

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:
C12N 15/31, 15/62, C07K 14/295, 16/12,
19/00, A01K 67/027, A61K 39/118,
G01N 33/53, C12Q 1/68

(11) International Publication Number: WO 99/28475
(43) International Publication Date: 10 June 1999 (10.06.99)

(21) International Application Number: PCT/IB98/01939

(22) International Filing Date: 27 November 1998 (27.11.98)

(30) Priority Data:

 97/15041
 28 November 1997 (28.11.97)
 FR

 97/16034
 17 December 1997 (17.12.97)
 FR

 60/107,077
 4 November 1998 (04.11.98)
 US

(71) Applicant (for all designated States except US): GENSET [FR/FR]; 24, rue Royale, F-75008 Paris (FR).

(72) Inventor: and

(75) Inventor/Applicant (for US only): GRIFFAIS, Rémy [FR/FR]; 51, boulevard Romain Roland, F-92120 Montrouge (FR).

(74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F-75116 Paris (FR). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: CHLAMYDIA TRACHOMATIS GENOMIC SEQUENCE AND POLYPEPTIDES, FRAGMENTS THEREOF AND USES THEREOF, IN PARTICULAR FOR THE DIAGNOSIS, PREVENTION AND TREATMENT OF INFECTION

(57) Abstract

The subject of the invention is the genomic sequence and the nucleotide sequences encoding polypeptides of Chlamydia trachomatis, such as cellular envelope polypeptides, which are secreted or specific, or which are involved in metabolism, in the replication process or in virulence, polypeptides encoded by such sequences, as well as vectors including the said sequences and cells or animals transformed with these vectors. The invention also relates to transcriptional gene products of the Chlamydia trachomatis genome, such as, for example, antisense and ribozyme molecules, which can be used to control growth of the microorganism. The invention also relates to methods of detecting these nucleic acids or polypeptides and kits for diagnosing Chlamydia trachomatis infection. The invention also relates to a method of selecting compounds capable of modulating bacterial infection and a method for the biosynthesis or biodegradation of molecules of interest using the said nucleotide sequences or the said polypeptides. The invention finally comprises, pharmaceutical, in particular vaccine, compositions for the prevention and/or treatment of bacterial, in particular Chlamydia trachomatis, infections.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	1E	Ireland	MN	Mongolia	ŲA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	18	Iceland	MW	Malawi	US	United States of Americ
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	L	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

WO 99/28475 PCT/IB98/01939

CHLAMYDIA TRACHOMATIS GENOMIC SEQUENCE AND POLYPEPTIDES, FRAGMENTS THEREOF AND USES THEREOF, IN PARTICULAR FOR THE DIAGNOSIS, PREVENTION AND TREATMENT OF INFECTION

5

25

The subject of the invention is the genomic sequence and the nucleotide sequences encoding polypeptides of *Chlamydia trachomatis*, such as cellular envelope polypeptides, which are secreted or specific, or which are involved in metabolism, in the replication process or in virulence, polypeptides encoded by such sequences as well as vectors including the said sequences and cells or animals transformed with these vectors. The invention also relates to transcriptional gene products of the *Chlamydia trachomatis* genome, such as, for example, antisense and ribozyme molecules, which can be used to control growth of the microorganism. The invention also relates to methods of detecting these nucleic acids or polypeptides and kits for diagnosing *Chlamydia trachomatis* infection. The invention also relates to a method of selecting compounds capable of modulating bacterial infection and a method for the biosynthesis or biodegradation of molecules of interest using the said nucleotide sequences or the said polypeptides. The invention finally comprises, pharmaceutical, in particular vaccine, compositions for the prevention and/or treatment of bacterial, in particular *Chlamydia trachomatis*, infections.

The genus Chlamydia is composed of four species: Chlamydia psittaci, Chlamydia 20 pecorum, Chlamydia pneumoniae and Chlamydia trachomatis.

Chlamydia psittaci comprises numerous species, whose hosts are terrestrial vertebrate animals as well as birds and occasionally humans;

Chlamydia pecorum is a pathogen of ruminants;

Chlamydia pneumoniae is responsible for pneumopathies, for sinusitis and for arterial impairments in humans;

Chlamydia trachomatis (Ct) is responsible for a large number of human diseases:

- eye diseases: conventional trachoma, nonendemic trachoma, paratrachoma, inclusion conjunctivitis in neonates and in adults;
- genital diseases: nongonococcal uretritis, epididymitis, cervicitis, salpingitis, perihepatitis and bartholinitis as well as pneumopathy in breast-feeding infants;
 - systemic diseases: venereal lymphogranulomatosis (LGV).

These diseases affect a very large number of women and men [more than 600 million individuals are trachoma carriers and there are more than 90 million cases of genital *Chlamydia* infections] worldwide. Accordingly, basic and applied research which makes it possible to understand the physiopathology linked to this bacterium is very important for public health. (Raulston JE., 1995; Hackstadt T. et al., 1996).

Eye impairments due to Chlamydia trachomatis cause trachoma and inclusion

conjunctivitis. Trachoma is a chronic conjunctivitis. It is the major cause of curable eye diseases leading to blindness. It is estimated that 20 million cases of loss of sight are due to it worldwide. Moreover, inclusion conjunctivitis is an eye inflammation which is caused by *Chlamydia trachomatis* and is transmitted by the venereal route. Inclusion conjunctivitis affects adults and neonates exposed to genital secretions.

Two types of eye disease caused by agents of the species Chlamydia trachomatis can be distinguished. The conventional trachomatous disease is found in endemic regions; transmission occurs from eye to eye and through the hands, or it can be passed on by flies. In nonendemic regions, transmission occurs through the genital apparatus; it usually only causes conjunctivitis, most often without associated keratitis; it is rare for a pannus or for scars similar to those in trachoma to develop. This conjunctival impairment is called paratrachoma to differentiate it from the conventional endemic trachoma which is transmitted by the ocular route. The seriousness and the number of cases of trachoma have decreased over the last forty years. This is related to the improvement in hygiene and living conditions. However, trachoma remains the principal cause of avoidable blindness in Africa, in the Middle East and in some regions of Asia. The transmission of the endemic disease occurs in particular through close personal contact, in regions where a secondary exposure exists in a repeated form. Often, the infection is also latent. In some industrialized countries, such as the United States, a mild form of trachoma still exists in some ethnic groups. Sometimes, a tardive trachoma may be found following an immunosuppressive treatment. The eye impairments caused by Chlamydia trachomatis, such as inclusion conjunctivitis and paratrachoma, are also a complication due to a common venereal infection. These infections are not very frequent; they occur most often in young adults. The eye impairments in neonates are produced during the passage through the maternal genital routes during childbirth. Theoretically, endemic trachoma and inclusion conjunctivitis in adults appear in the form of conjunctivitis, the latter being characterized by the presence of lymphoid follicles. In regions where the endemic disease is serious, the disease often starts before the age of 2 years and reinfection is frequent. Superficial neovascularization is added, in this case, to leukocytic infiltration. The conjunctival scars will then cause trichiasis and entropion. The eroded cornea will become a carrier of a corneal ulcer of bacterial origin. The scar on the cornea causes blindness. Impairment of the lachrymal glands gives a picture of dryness of the cornea. Xerosis becomes complicated with secondary bacterial ulcer. In regions where trachoma is endemic, the infectious process disappears towards the age of fifteen. The scars then progress to blindness, which affects almost exclusively adults. In regions where exposure is lower, the infectious process is, in this case, less rapid and adults are carriers of a chronic disease.

Positive diagnosis of trachoma can be most often established by clinical observation: lymphoid follicles are visible on the upper tarsal conjuctiva; conjunctival scar is typical. Vascular

pannus exists. In endemic regions, clinical diagnosis is often sufficient. However, isolated cases of inclusion conjunctivitis must be the subject of a differential diagnosis, in particular to distinguish viral conjunctivitis.

Public health measures against the endemic form of the disease provide for mass treatments with tetracycline or erythromycin collyria of all children. The treatment may also provide for surgical correction of the lesions. The other conjunctival impairments respond well to general treatments with tetracyclines or erythromycin. The prevention of trachomatous disease by health measures and by improving living standards is sufficient. Furthermore, to avoid the spread of trachoma, antibiotic collyria may be used.

The role of *Chlamydia trachomatis* in a number of genital impairments has been demonstrated over the last three decades. *Chlamydia trachomatis* is responsible in this case for a pathology which may be superposed on the impairments observed with *Neisseria gonorrhoeae*. The pathologies for which *Chlamydia trachomatis* may be responsible at the genital level are acquired by the venereal route and are a major source of sexually transmitted diseases.

The epidemiology of *Chlamydia trachomatis* genital infections shows each year more than 4 million new cases in the United States, and more than 3 million new cases in Europe. Like the other venereal infections, *Chlamydia trachomatis* affects young subjects. There is a direct relationship between the number of sexual partners and the frequency of the disease. For example, the frequency of *Chlamydia trachomatis* appears to be five to ten times higher than that of *Neisseria gonorrhoeae* in pregnant women. The *Chlamydia trachomatis* infection is probably more discreet than its *Neisseria gonorrhoeae* homologue. This relative clinical silence, estimated in women at 50% or even 70% of infections, explains why the total morbidity of *Chlamydia trachomatis* conditions is high. Diagnosis must therefore be requested in patients who are sometimes asymptomatic carriers of infection.

Chlamydia trachomatis is responsible for nearly 30% of nongonococcal urethritis, or NGU. Chlamydia trachomatis urethritis may be discreet, the disease then progresses to a certain form of chronicity. The diagnosis will, like for the other clinical forms of the disease, be called into play later.

Chlamydia trachomatis is a cause of epididymitis in humans during a period of sexual activity. The bacterium may be found in the urethra, urine, sperm or even a sample collected by aspiration from the epididymis. It is in particular found in humans under 35 years of age. A discharge from the urethra which is associated with the disease suggests the diagnosis of a Chlamydia condition or sometimes a gonococcal condition.

Untreated Reiter's syndrome, if accompanied by urethritis, evokes a Chlamydia trachomatis condition.

10

15

20

WO 99/28475 PCT/IB98/01939

4

gonorrhoea (or have had contact), 10% to 20% of women having a venereal origin, 5% of women consulting having no particular origin.

The cervix is often normal during a Chlamydia trachomatis infection. However, a hypertrophic cervical erythema will cause such an infection to be suspected. Chlamydia trachomatis is responsible for an endocervicitis whereas viral impairments result in exocervicitis. A nongonococcal endocervicitis requires treating the patient and partners with tetracyclines.

Chlamydia trachomatis is responsible for a large number of acute salpingites. The picture is often complicated by an acute peritonitis or even a perihepatitis.

In case of pregnancy, the risk is first that of infection of the neonate at birth. However, the risk of postpartum complications exists (endometritis or salpingitis).

The reference method for the diagnosis of *Chlamydia trachomatis* is the isolation of the bacterium on cell culture. For all infections, the sample collection should make it possible to obtain a suitable sample with the aid of a swab. This sample should be transported to a laboratory under excellent conditions; in particular, the cold chain must absolutely be maintained. The placing in cell culture on mouse fibroblasts will be carried out by people having specific skills. The distinction of *Chlamydia trachomatis* with labelled antibodies and the observation of cell cultures under a microscope will take place two days after placing in culture. Provided these imperatives are observed, cell culture is a reliable technique. However, the constraints linked to this technique are many: not only must the laboratory be equipped for the cell culture, but, furthermore, highly competent staff must take care of this type of diagnosis.

Techniques for identifying genetic material can obviously be used for the detection of *Chlamydia trachomatis*. Among these techniques, enzymatic gene amplification or PCR is favoured by those skilled in the art. The technique indeed makes it possible to identify *Chlamydia trachomatis* with a very high sensitivity and complete specificity. Initially used in specialist laboratories, PCR is now performed in numerous medical laboratories. This diagnostic approach is important because it allows detection of the bacteria even in samples which have been transported under poor conditions.

The treatment of *Chlamydia* urethritis with antibiotics such as tetracycline or quinolones is very effective. The duration of treatment varies between 7 and 14 days. The treatment of pregnant women poses the problem of contraindications to tetracycline.

30

Neonatal infections caused by *Chlamydia trachomatis* are explained by the frequency of these bacteria in the cervix. In some studies, 5% to 13% of impairments are observed in the cervix in asymptomatic pregnant women. The neonates risk, in this case, developing an inclusion conjunctivitis. Not only can *Chlamydia trachomatis* be isolated from the children's eyes, but also persistently from the rhinopharynx and also from the rectum. Pneumopathies and otitis media are also found, a result of contamination at childbirth.

WO 99/28475 PCT/IB98/01939

5

Differential diagnosis of inclusion conjunctivitis in neonates is required with gonococcal ophthalmia; while the duration of incubation is from one to three days in the case of a gonococcal ophthalmia, neonatal inclusion conjunctivitis has an acute beginning with discharge and formation of membranes or even of conjunctival scars.

Treatment consists of oral erythromycin at the dose of 40 to 50 mg per kg of weight, for two to three weeks. In a nonendemic trachoma region, this disease never progresses to chronicity.

5

10

20

30

35

Finally, mention should be made of infantile pneumopathy. The syndrome is well defined; it is found in children affected by *Chlamydia trachomatis*. Less than ten children are affected by *Chlamydia trachomatis* pneumopathies per thousand births. The syndrome is, in this case, always found at an early age (less than four months).

Venereal lymphogranulomatosis is an infection which is transmitted through sexual contact and is due to *Chlamydia trachomatis* strains L1, L2 and L3. In humans, a passing primary genital lesion is followed by an often suppurative and multiple regional lymphadenopathy. This disease is a general disease which is accompanied by fever and a rise in the number of white blood cells. If it progresses to chronicity, the disease then becomes complicated with genital elephantiasis, stricture or even fistula of the genital apparatus, of the penis, of the urethra and of the rectum.

The three Chlamydia trachomatis strains L1, L2 and L3 are responsible for venereal lymphogranulomatosis. These Chlamydia strains are more virulent than the strains responsible for trachoma and STD. It is very important to note that venereal lymphogranulomatosis is a systemic disease which affects primarily the lymphatic tissue. Generally transmitted by the sexual route, Chlamydia trachomatis L may also cause contamination through direct contact or even during poor laboratory handling. In spite of these variable modes of transmission, the age for the highest incidence of these diseases corresponds to that for greater sexual activity. Venereal lymphogranulomatosis is still endemic in South America, in Africa and sometimes in Asia. For a long time, the prevalence of venereal lymphogranulomatosis was difficult to establish because of the difficulty of performing diagnosis with certitude. It should also be noted that men are affected more often than women. In low endemic regions, it is difficult to recognize the reservoir of microbes. This situation is explained by the fact that the isolation of the strains causing venereal lymphogranulomatoses from asymptomatic subjects is rarely successful.

Clinical impairment by venereal lymphogranulomatosis manifests itself by the appearance of a small ulcer 3 to 21 days after the exposure of small nonpainful vesicles. In both men and women, the lesion is most often silent. Since this impairment disappears within a few days and causes no functional discomfort and leaves no visible scar, the disease is often recognized late. The venereal lymphogranulomatosis strains may be found in the urethra or the endocervix in patients with inguinal adenopathies; these regions are then considered as the initial site of infection. The

25

30

35

characteristic feature of the venereal lymphogranulomatosis strains is that from the initial site of infection, *Chlamydia* exhibits a diffusion drained by the lymphatic ducts. The disease is then complicated by a ganglionic impairment of the region draining the site of inoculation. By way of example, anorectal infection causes deep adenopathies. These adneopathies are marked by the appearance of a periadenitis which forms a fluctuating and suppurative ganglionic mass. Fistulae will appear during the decline of the disease. As general signs are present at this stage of the disease, it is often confused with a malignant lymphoma. The other general complications are rarely observed. Clinical examinations have been able to lead biologists to isolate *Chlamydia* from the cerebrospinal fluid or from the blood. It should also be noted that in a number of cases (5%), venereal lymphogranulomatosis is complicated by a chronic oedema: this is genital elephantiasis.

The diagnosis of venereal lymphogranulomatosis requires the isolation of the *Chlamydia* strains involved in the disease. However, isolation on cell cultures is rarely used, but immunological reactions may be used.

The treatment of venereal lymphogranulomatosis in its initial phase is identical to the treatment of other *Chlamydia* infections. In the chronic phases, antibiotics have little effect on the progress of the disease, but they are however useful in case of superinfection. Although the recommended therapeutic arsenal is identical, it is advisable to prolong the treatment for a period of at least four weeks. In addition to this treatment, reconstructive surgery may be useful in cases of urethral, penile or rectal strictures, as well as for the treatment of fistulae.

In conclusion, a short and effective treatment, without recurrences, and a well-tolerated treatment of *Chlamydia trachomatis* infections therefore remains desirable.

An even greater need up until now relates to a diagnosis which is specific to each of the strains, which is sensitive, which can be carried out conveniently and rapidly, and which allows early detection of the infection.

No vaccine is currently available against *Chlamydia trachomatis*. The role of the immune defense in the physiology and pathology of the disease should probably be understood in order to develop satisfactory vaccines.

More detailed information relating to the biology of these strains, their interactions with their hosts, the associated phenomena of infectivity and those of escaping the immune defenses of the host in particular, and finally their involvement in the development of the these associated pathologies, will allow a better understanding of these mechanisms. In the light of the preceding text which shows in particular the limitations of the means of controlling *Chlamydia trachomatis* infection, it is therefore at present essential, on the one hand, to develop molecular tools, in particular from a better genetic knowledge of *Chlamydia trachomatis*, but also to develop new preventive and therapeutic treatments, new diagnostic methods and new vaccine strategies which are specific,

20

30

35

effective and tolerated. This is precisely the object of the present invention.

The subject of the present invention is the nucleotide sequence having the sequence SEQ ID No. 1 of the *Chlamydia trachomatis LGV2* genome. However, the invention is not limited to SEQ ID No. 1, but encompasses genomes and nucleotides encoding polypeptides of strain variants, polymorphisms, allelic variants, and mutants.

Thus, the subject of the present invention encompasses nucleotide sequences characterized in that they are chosen from:

- a) the nucleotide sequence of SEQ ID No. 1, a nucleotide sequence exhibiting at least 99.9% identity with the sequence SEQ ID No. 1, the nucleotide sequence of the genomic DNA contained within ECACC Deposit No. 98112618, the nucleotide sequence of a clone insert within ECACC Deposit No. 98112617 (these being provisional deposit numbers);
 - b) a nucleotide sequence homologous to the sequence SEQ ID No. 1;
- c) a polynucleotide sequence that hybridizes to the nucleotide sequence of a) under conditions of high or intermediate stringency as described below:
- (i) By way of example and not limitation, procedures using conditions of high stringency are as follows: Prehybridization of filters containing DNA is carried out for 8 h to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65°C, the preferred hybridization temperature, in prehybridization mixture containing 100 µg/ml denatured salmon sperm DNA and 5-20 X 10⁶ cpm of ³²P-labeled probe. Alternatively, the hybridization step can be performed at 65°C in the presence of SSC buffer, 1 x SSC corresponding to 0.15M NaCl and 0.05 M Na citrate. Subsequently, filter washes can be done at 37°C for 1 h in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA, followed by a wash in 0.1X SSC at 50°C for 45 min. Alternatively, filter washes can be performed in a solution containing 2 x SSC and 0.1% SDS, or 0.5 x SSC and 0.1% SDS, or 0.1 x SSC and 0.1% SDS at 68°C for 15 minute intervals. Following the wash steps, the hybridized probes are detectable by autoradiography. Other conditions of high stringency which may be used are well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety.
- (ii) By way of example and not limitation, procedures using conditions of intermediate stringency are as follows: Filters containing DNA are prehybridized, and then hybridized at a temperature of 60°C in the presence of a 5 x SSC buffer and labeled probe. Subsequently, filters washes are performed in a solution containing 2x SSC at 50°C and the hybridized probes are detectable by autoradiography. Other conditions of intermediate stringency which may be used are

10

20

25

well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety.

- d) a nucleotide sequence complementary to the sequence SEQ ID No. 1 or complementary to a nucleotide sequence as defined in a), b) or c), and a nucleotide sequence of their corresponding RNA;
- e) a nucleotide sequence of a representative fragment of the sequence SEQ ID No. 1, or of a representative fragment of the nucleotide sequence as defined in a), b), c) or d);
 - f) a nucleotide sequence comprising a sequence as defined in a), b), c), d) or e);
- g) a nucleotide sequence capable of being obtained from a nucleotide sequence as defined in a), b), c), d), e) or f); and
- h) a modified nucleotide sequence of a nucleotide sequence as defined in a), b), c), d), e), f) or g).
- Sequence of the genome, or genomic sequence of *Chlamydia trachomatis* is understood to mean the sequence of the chromosome of *Chlamydia trachomatis*, in contrast with the plasmid sequence of *Chlamydia trachomatis*.

Nucleotide sequence, polynucleotide or nucleic acid are understood to mean, according to the present invention, either a double-stranded DNA, a single-stranded DNA or products of transcription of the said DNAs.

It should be understood that the present invention does not relate to the genomic nucleotide sequences of *Chlamydia trachomatis* taken in their natural environment, that is to say in the natural state. They are sequences which may have been isolated, purified or partially purified, by separation methods such as, for example, ion-exchange chromatography, molecular size exclusion chromatography or affinity chromatography, or alternatively fractionation techniques based on solubility in various solvents, or by genetic engineering methods such as amplification, cloning or subcloning, it being possible for the sequences of the invention to be carried by vectors.

The nucleotide sequence SEQ ID No. 1 was obtained by sequencing the *Chlamydia* trachomatis LGV2 genome by the method of directed sequencing after fluorescent automated sequencing of the inserts of clones and assembling of these sequences of nucleotide fragments (inserts) by means of softwares (cf. Examples). In spite of the high precision of the sequence SEQ ID No. 1, it is possible that it does not perfectly, 100% represent the nucleotide sequence of the *Chlamydia trachomatis LGV2* genome and that a few rare sequencing errors or uncertainties still remain in the sequence SEQ ID No. 1. In the present invention, the presence of an uncertainty for an amino acid is designated by «Xaa» and that for a nucleotide is designated by «N» in the sequence

WO 99/28475 PCT/IB98/01939

9

listing below. These few rare errors or uncertainties could be easily detected and corrected by persons skilled in the art using the entire chromosome and/or its representative fragments according to the invention and standard amplification, cloning and sequencing methods, it being possible for the sequences obtained to be easily compared, in particular by means of a computer software and using computer-readable media for recording the sequences according to the invention as described, for example, below. After correcting these possible rare errors or uncertainties, the corrected nucleotide sequence obtained would still exhibit at least 99.9% identity with the sequence SEQ ID No. 1. Such rare sequencing uncertainties are not present within the DNA contained within ECACC Deposit No. 98112617 or 98112618 (provisional numbers) and whatever rare sequence uncertainties that exist within SEQ ID No. 1 can routinely be corrected utilizing the DNA of the ECACC Deposits.

10

Homologous nucleotide sequence for the purposes of the present invention is understood to mean a nucleotide sequence having a percentage identity with the bases of the nucleotide sequence SEQ ID No. 1 of at least 80%, preferably 90% and 95%, this percentage being purely statistical and it being possible for the differences between the two nucleotide sequences to be distributed randomly and over their entire length. The said homologous sequences exhibiting a percentage identity with the bases of the nucleotide sequence SEQ ID No. 1 of at least 80%, preferably 90% and 95%, may comprise, for example, the sequences corresponding to the genomic sequence or to the sequences of its representative fragments of a bacterium belonging to the Chlamydia family, including the species Chlamydia pneumoniae, Chlamydia psittaci and Chlamydia pecorum mentioned above, as well as the sequences corresponding to the genomic sequence or to the sequences of its representative fragments of a bacterium belonging to the variants of the species Chlamydia trachomatis. In the present invention, the terms family and genus are mutually interchangeable, the terms variant, serotype, strain and subspecies are also mutually interchangeable. These homologous sequences may thus correspond to variations linked to mutations within the same species or between species and may correspond in particular to truncations, substitutions, deletions and/or additions of at least one nucleotide. The said homologous sequences may also correspond to variations linked to the degeneracy of the genetic code or to a bias in the genetic code which is specific to the family, to the species or to the variant and which are likely to be present in Chlamydia.

Protein and/or nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (Pearson and Lipman, 1988, Proc. Natl. Acad. Sci. USA 85(8):2444-2448; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Thompson et al., 1994, Nucleic Acids Res. 22(2):4673-4680; Higgins et al., 1996, Methods Enzymol. 266:383-402; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Altschul et al., 1993, Nature Genetics 3:266-272).

25

30

In a particularly preferred embodiment, protein and nucleic acid sequence homologies are evaluated using the Basic Local Alignment Search Tool ("BLAST") which is well known in the art (see, e.g., Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268; Altschul et al., 1990, J. Mol. Biol. 215:403-410; Altschul et al., 1993, Nature Genetics 3:266-272; Altschul et al., 1997, Nuc. Acids Res. 25:3389-3402). In particular, five specific BLAST programs are used to perform the following task:

- (1)BLASTP and BLAST3 compare an amino acid query sequence against a protein sequence database;
 - (2)BLASTN compares a nucleotide query sequence against a nucleotide sequence database;
- (3)BLASTX compares the six-frame conceptual translation products of a query nucleotide sequence (both strands) against a protein sequence database;
- (4)TBLASTN compares a query protein sequence against a nucleotide sequence database translated in all six reading frames (both strands); and
- (5)TBLASTX compares the six-frame translations of a nucleotide query sequence against the six-frame translations of a nucleotide sequence database.

The BLAST programs identify homologous sequences by identifying similar segments, which are referred to herein as "high-scoring segment pairs," between a query amino or nucleic acid sequence and a test sequence which is preferably obtained from a protein or nucleic acid sequence database. High-scoring segment pairs are preferably identified (i.e., aligned) by means of a scoring matrix, many of which are known in the art. Preferably, the scoring matrix used is the BLOSUM62 matrix (Gonnet et al., 1992, Science 256:1443-1445; Henikoff and Henikoff, 1993, Proteins 17:49-61). Less preferably, the PAM or PAM250 matrices may also be used (see, e.g., Schwartz and Dayhoff, eds., 1978, Matrices for Detecting Distance Relationships: Atlas of Protein Sequence and Structure, Washington: National Biomedical Research Foundation)

The BLAST programs evaluate the statistical significance of all high-scoring segment pairs identified, and preferably selects those segments which satisfy a user-specified threshold of significance, such as a user-specified percent homology. Preferably, the statistical significance of a high-scoring segment pair is evaluated using the statistical significance formula of Karlin (see, e.g., Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268).

Nucleotide sequence complementary to a sequence of the invention is understood to mean any DNA whose nucleotides are complementary to those of the sequence of the invention, and whose orientation is reversed (antiparallel sequence).

The present invention further comprises fragments of the sequences of a) through h) above. Representative fragments of the sequences according to the invention will be understood to mean any nucleotide fragment having at least 8 successive nucleotides, preferably at least 12

15

20

30

35

successive nucleotides, and still more preferably at least 15 or at least 20 successive nucleotides of the sequence from which it is derived. It is understood that such fragments refer only to portions of SEQ ID No. 1 that are not currently listed in a publicly available database.

Among these representative fragments, those capable of hybridizing under stringent conditions with a nucleotide sequence according to the invention are preferred. Hybridization under stringent conditions means that the temperature and ionic strength conditions are chosen such that they allow hybridization to be maintained between two complementary DNA fragments.

By way of illustration, high stringency conditions for the hybridization step for the purposes of defining the nucleotide fragments described above, are advantageously the following.

The hybridization is carried out at a preferred temperature of 65°C in the presence of SSC buffer, 1 x SSC corresponding to 0.15 M NaCl and 0.05 M Na citrate. The washing steps may be, for example, the following:

 $2 \times SSC$, 0.1% SDS at room temperature followed by three washes with $1 \times SSC$, 0.1% SDS; 0.5 x SSC, 0.1% SDS; 0.1 x SSC, 0.1% SDS at 68°C for 15 minutes.

Intermediate stringency conditions, using, for example, a temperature of 60°C in the presence of a 5 x SSC buffer, or of low stringency, for example a temperature of 50°C in the presence of a 5 x SSC buffer, respectively require a lower overall complementarity for the hybridization between the two sequences.

The stringent hybridization conditions described above for a polynucleotide of about 300 bases in size will be adapted by persons skilled in the art for larger- or smaller-sized oligonucleotides, according to the teaching of Sambrook et al., 1989.

Among the representative fragments according to the invention, those which can be used as primer or probe in methods which make it possible to obtain homologous sequences or their representative fragments according to the invention, or to reconstitute a genomic fragment found to be incomplete in the sequence SEQ ID No. 1 or carrying an error or an uncertainty, are also preferred, these methods, such as the polymerase chain reaction (PCR), cloning and sequencing of nucleic acid being well known to persons skilled in the art. These homologous nucleotide sequences corresponding to mutations or to inter- or intra-species variations, as well as the complete genomic sequence or one of its representative fragments capable of being reconstituted, of course form part of the invention.

Among the said representative fragments, those which can be used as primer or probe in methods allowing diagnosis of the presence of *Chlamydia trachomatis* or one of its associated microorganisms as defined below are also preferred.

The representative fragments capable of modulating, regulating, inhibiting or inducing the expression of a gene of *Chlamydia trachomatis* or one of its associated microorganisms, and/or capable of modulating the replication cycle of *Chlamydia trachomatis* or one of its associated

microorganisms in the host cell and/or organism, are also preferred. Replication cycle is intended to designate invasion, multiplication, intracellular localization, in particular retention in the vacuole and inhibition of the process of fusion to the lysosome, and propagation of *Chlamydia trachomatis* or one of its associated microorganisms from host cells to host cells.

Among the said representative fragments, those corresponding to nucleotide sequences corresponding to open reading frames, called ORF sequences (ORF for open reading frame), and encoding polypeptides, such as for example, but without being limited thereto, the ORF sequences which will be later described, are finally preferred.

The representative fragments according to the invention may be obtained, for example, by specific amplification, such as PCR, or after digestion, with appropriate restriction enzymes, of nucleotide sequences according to the invention; these methods are in particular described in the manual by Sambrook et al., 1989. The said representative fragments may also be obtained by chemical synthesis when they are not too large in size and according to methods well known to persons skilled in the art. For example, such fragments can be obtained by isolating fragments of the genomic DNA of ECACC Deposit No. 98112618 or a clone insert present at this ECACC Deposit No. 98112617 (provisional numbers).

The representative fragments according to the invention may be used, for example, as primer, to reconstitute some of the said representative fragments, in particular those in which a portion of the sequence is likely to be missing or imperfect, by methods well known to persons skilled in the art such as amplification, cloning or sequencing techniques.

Modified nucleotide sequence will be understood to mean any nucleotide sequence obtained by mutagenesis according to techniques well known to persons skilled in the art, and exhibiting modifications in relation to the normal sequences, for example mutations in the regulatory and/or promoter sequences for the expression of a polypeptide, in particular leading to a modification of the level of expression of the said polypeptide or to a modulation of the replicative cycle.

Modified nucleotide sequence will also be understood to mean any nucleotide sequence encoding a modified polypeptide as defined below.

The subject of the present invention also includes *Chlamydia trachomatis* nucleotide sequences characterized in that they are chosen from a nucleotide sequence of an open reading frame (ORF), that is, the ORF2 to ORF1197 sequences.

The ORF2 to ORF1197 nucleotide sequences are defined in Tables 1 and 2, *infra*, represented below by their position on the sequence SEQ ID No. 1. For example, the ORF10 sequence is defined by the nucleotide sequence between the nucleotides at position 9828 and 10430 on the sequence SEQ ID No. 1, ends included. ORF2 to ORF1197 have been identified via homology analyses as well as via analyses of potential ORF start sites, as discussed in the examples

below. It is to be understood that each identified ORF of the invention comprises a nucleotide sequence that spans the contiguous nucleotide sequence from the codon immediately 3' to the stop codon of the preceding ORF and through the 5' codon to the next stop codon of SEQ ID No.:1 inframe to the ORF nucleotide sequence. Table 2, *infra*, lists the beginning, end and potential start site of each of ORFs 2-1197. In one embodiment, the ORF comprises the contiguous nucleotide sequence spanning from the potential ORF start site downstream (that is, 3') to the ORF stop codon (or the ORF codon immediately adjacent to and upstream of the ORF stop codon). ORF2 to ORF1197 encode the polypeptides of SEQ ID No. 2 to SEQ ID No. 1197.

Upon introduction of minor frameshifts, certain individual ORFs can comprise larger combined ORFs. A list of such putative "combined" ORFs is shown in Table 3, below. For example, a combined ORF can comprise ORF 1076 and ORF 1073, including intervening in-frame, nucleotide sequences. The order of ORFs (5' to 3'), within each "combined" ORF is as listed. It is to be understood that when ORF2 to ORF1197 are referred to herein, such reference is also meant to include "combined" ORFs. Polypeptide sequences encoded by such "combined" ORFs are also part of the present invention.

```
Table 3
    ORF 1076, ORF 1073;
    ORF 3, ORF 2;
    ORF 23, ORF 22, ORF 21;
   ORF 1141, ORF 477, ORF 478, ORF 479;
    ORF 487, ORF 486, ORF 485, ORF 484, ORF 483, ORF 482, ORF 481;
    ORF 488, ORF 489;
    ORF 573, ORF 572, ORF 571;
    ORF 817, ORF 818;
25 ORF 819, ORF 820;
    ORF 1037, ORF 1038;
    ORF 1071, ORF 1070;
    ORF 17, ORF 1077;
    ORF 1185, ORF 933, ORF 934;
30 ORF 1060, ORF 1059;
    ORF 155, ORF 156;
    ORF 679, ORF 680;
    ORF 879, ORF 878;
```

ORF 1028; ORF 1029, and representative fragments.

Table 1 also depicts the results of homology searches that compared the sequences of the polypeptides encoded by each of the ORFs to sequences present in public published databases. It is understood that in one embodiment, those polypeptides listed in Table 1 as exhibiting greater than about 95% identity to a polypeptide present in a publicly disclosed database are not considered part of the present invention; likewise in this embodiment, those nucleotide sequences encoding such polypeptides are not considered part of the invention. In another embodiment, it is understood that those polypeptides listed in Table 1 as exhibiting greater than about 99% identity to a polypeptide present in a publicly disclosed database are not considered part of the invention; likewise, in this embodiment, those nucleotide sequences encoding such polypeptides are not considered part of the 10 invention.

The invention also relates to the nucleotide sequences characterized in that they comprise a nucleotide sequence chosen from:

- an ORF2 to ORF1197, a «combined» ORF nucleotide sequence, the nucleotide sequence of the genomic DNA contained within ECACC Deposit No. 98112618 or the nucleotide sequence of a clone insert in ECACC Deposit No. 98112617 according to the invention;
- a homologous nucleotide sequence exhibiting at least 80% identity across an entire b) ORF2 to ORF1197 nucleotide sequence according to the invention or as defined in a);
- a polynucleotide sequence that hybridizes to ORF2 to ORF1197 under conditions of c) high or intermediate stringency as described below:
- (i) By way of example and not limitation, procedures using conditions of high stringency are as follows: Prehybridization of filters containing DNA is carried out for 8 h to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65°C, the preferred hybridization temperature, in prehybridization mixture containing 100 μg/ml denatured salmon sperm DNA and 5-20 X 10⁶ cpm of ³²P-labeled probe. Alternatively, the 25 hybridization step can be performed at 65°C in the presence of SSC buffer, 1 x SSC corresponding to 0.15M NaCl and 0.05 M Na citrate. Subsequently, filter washes can be done at 37°C for 1 h in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA, followed by a wash in 0.1X SSC at 50°C for 45 min. Alternatively, filter washes can be performed in a solution containing 2 x SSC and 0.1% SDS, or 0.5 x SSC and 0.1% SDS, or 0.1 x SSC and 0.1% SDS at 68°C for 15 minute 30 intervals. Following the wash steps, the hybridized probes are detectable by autoradiography. Other conditions of high stringency which may be used are well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety.

Preferably, such sequences encode a homolog of a polypeptide encoded by one of ORF2 to ORF1197. In one embodiment, such sequences encode a *Chlamydia trachomatis* polypeptide.

- (ii) By way of example and not limitation, procedures using conditions of intermediate stringency are as follows: Filters containing DNA are prehybridized, and then hybridized at a temperature of 60°C in the presence of a 5 x SSC buffer and labeled probe. Subsequently, filters washes are performed in a solution containing 2x SSC at 50°C and the hybridized probes are detectable by autoradiography. Other conditions of intermediate stringency which may be used are well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989,
 10 Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety. Preferably, such sequences encode a homolog of a polypeptide encoded by one of ORF2 to ORF1197. In one embodiment, such sequences encode a Chlamydia trachomatis polypeptide.
- d) a complementary or RNA nucleotide sequence corresponding to an ORF2 to ORF1197 sequence according to the invention or as defined in a), b) or c);
 - e) a nucleotide sequence of a representative fragment of an ORF2 to ORF1197 sequence according to the invention or of a sequence as defined in a), b), c) or d);
 - f) a nucleotide sequence capable of being obtained from an ORF2 to ORF1197 sequence according to the invention or as defined in a), b), c), d) or e); and
- g) a modified nucleotide sequence of an ORF2 to ORF1197 sequence according to the invention or as defined in a), b), c), d), e) or f).

As regards the homology with the ORF2 to ORF1197 nucleotide sequences, the homologous sequences exhibiting a percentage identity with the bases of one of the ORF2 to ORF1197 nucleotide sequences of at least 80%, preferably 90% and 95%, are preferred. Such homologous sequences are identified routinely via, for example, the algorithms described above and in the examples below. The said homologous sequences correspond to the homologous sequences as defined above and may comprise, for example, the sequences corresponding to the ORF sequences of a bacterium belonging to the Chlamydia family, including the species Chlamydia pneumoniae, Chlamydia psittaci and Chlamydia pecorum mentioned above, as well as the sequences corresponding to the ORF sequences of a bacterium belonging to the variants of the species Chlamydia trachomatis. These homologous sequences may likewise correspond to variations linked to mutations within the same species or between species and may correspond in particular to truncations, substitutions, deletions and/or additions of at least one nucleotide. The said homologous sequences may also correspond to variations linked to the degeneracy of the genetic code or to a bias in the genetic code which is specific to the family, to the species or to the variant and which are likely to be present in

Chlamydia.

35

The invention comprises the polypeptides encoded by a nucleotide sequence according to the invention, preferably by a representative fragment of the sequence SEQ ID No. 1 and corresponding to an ORF sequence, in particular the *Chlamydia trachomatis* polypeptides, characterized in that they are chosen from the sequences SEQ ID No. 2 to SEQ ID No. 1197, and representative fragments thereof. However, the invention is not limited to polypeptides encoded by ORFs in SEQ ID No. 1 and its corresponding ORF sequences, but encompasses polypeptides of strain variants, polymorphisms, allelic variants, and mutants.

Thus, the invention also comprises the polypeptides characterized in that they comprise a polypeptide chosen from:

- a) a polypeptide encoded by a polynucleotide sequence in SEQ ID No. 1 (e.g., any polypeptide encoded by a polynucleotide sequence corresponding to ORF2 to ORF1197) and/or representative fragments thereof according to the invention;
- a polypeptide homologous to a polypeptide according to the invention, or as defined
 in a);
 - c) a polypeptide encoded by a polynucleotide sequence that hybridizes to SEQ ID No. 1 or ORF2 to ORF1197 under high or intermediate stringency as described below:
 - (i) By way of example and not limitation, procedures using conditions of high stringency are as follows: Prehybridization of filters containing DNA is carried out for 8 h to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65°C, the preferred hybridization temperature, in prehybridization mixture containing 100 μg/ml denatured salmon sperm DNA and 5-20 X 106 cpm of ³²P-labeled probe. Alternatively, the hybridization step can be performed at 65°C in the presence of SSC buffer, 1 x SSC corresponding to 0.15M NaCl and 0.05 M Na citrate. Subsequently, filter washes can be done at 37°C for 1 h in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA, followed by a wash in 0.1X SSC at 50°C for 45 min. Alternatively, filter washes can be performed in a solution containing 2 x SSC and 0.1% SDS, or 0.5 x SSC and 0.1% SDS, or 0.1 x SSC and 0.1% SDS at 68°C for 15 minute intervals. Following the wash steps, the hybridized probes are detectable by autoradiography. Other conditions of high stringency which may be used are well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety. Preferably, such sequences encode a homolog of a polypeptide encoded by one of ORF2 to ORF1197 . In one embodiment, such sequences encode a Chlamydia trachomatis polypeptide.

20

25

35

- (ii) By way of example and not limitation, procedures using conditions of intermediate stringency are as follows: Filters containing DNA are prehybridized, and then hybridized at a temperature of 60°C in the presence of a 5 x SSC buffer and labeled probe. Subsequently, filters washes are performed in a solution containing 2x SSC at 50°C and the hybridized probes are detectable by autoradiography. Other conditions of intermediate stringency which may be used are well known in the art and as cited in Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Press, N.Y., pp. 9.47-9.57; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. are incorporated herein in their entirety. Preferably, such sequences encode a homolog of a polypeptide encoded by one of ORF2 to ORF1197. In one embodiment, such sequences encode a Chlamydia trachomatis polypeptide.
- d) a fragment of at least 5 amino acids of a polypeptide according to the invention, or as defined in a), b) or c);
- e) a biologically active fragment of a polypeptide according to the invention, or as 5 defined in a), b), c) or d); and
 - f) a modified polypeptide of a polypeptide according to the invention, as defined in a), b), c), d) or e).

In the present description, the terms polypeptide, peptide and protein are interchangeable.

It should be understood that the invention does not relate to the polypeptides in natural form, that is to say that they are not taken in their natural environment but that they may have been isolated or obtained by purification from natural sources, or alternatively obtained by genetic recombination, or else by chemical synthesis and that they may, in this case, comprise nonnatural amino acids, as will be described below.

Homologous polypeptide will be understood to designate the polypeptides exhibiting, in relation to the natural polypeptide, certain modifications such as in particular a deletion, addition or substitution of at least one amino acid, a truncation, an extension, a chimeric fusion, and/or a mutation, or polypeptides exhibiting post-translational modifications. Among the homologous polypeptides, those whose amino acid sequence exhibits at least 80%, preferably 90%, homology or identity with the amino acid sequences of the polypeptides according to the invention are preferred. In the case of a substitution, one or more consecutive or nonconsecutive amino acids are replaced by "equivalent" amino acids. The expression "equivalent" amino acid is intended here to designate any amino acid capable of being substituted for one of the amino acids in the basic structure without, however, essentially modifying the biological activities of the corresponding peptides and as will be defined later.

Protein and/or nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (Pearson and Lipman, 1988, Proc. Natl. Acad. Sci. USA 85(8):2444-2448; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Thompson et al., 1994, Nucleic Acids Res. 22(2):4673-4680; Higgins et al., 1996, Methods Enzymol. 266:383-402; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Altschul et al., 1993, Nature Genetics 3:266-272).

In a particularly preferred embodiment, protein and nucleic acid sequence homologies are evaluated using the Basic Local Alignment Search Tool ("BLAST") which is well know in the art (see, e.g., Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268; Altschul et al., 1990, J. Mol. Biol. 215:403-410; Altschul et al., 1993, Nature Genetics 3:266-272; Altschul et al., 1997, Nuc. Acids Res. 25:3389-3402). In particular, five specific BLAST programs are used to perform the following task:

- (1)BLASTP and BLAST3 compare an amino acid query sequence against a protein sequence 15 database;
 - (2)BLASTN compares a nucleotide query sequence against a nucleotide sequence database;
 - (3)BLASTX compares the six-frame conceptual translation products of a query nucleotide sequence (both strands) against a protein sequence database;
- (4)TBLASTN compares a query protein sequence against a nucleotide sequence database translated in all six reading frames (both strands); and
 - (5)TBLASTX compares the six-frame translations of a nucleotide query sequence against the six-frame translations of a nucleotide sequence database.

The BLAST programs identify homologous sequences by identifying similar segments, which are referred to herein as "high-scoring segment pairs," between a query amino or nucleic acid sequence and a test sequence which is preferably obtained from a protein or nucleic acid sequence database. High-scoring segment pairs are preferably identified (i.e., aligned) by means of a scoring matrix, many of which are known in the art. Preferably, the scoring matrix used is the BLOSUM62 matrix (Gonnet et al., 1992, Science 256:1443-1445; Henikoff and Henikoff, 1993, Proteins 17:49-61). Less preferably, the PAM or PAM250 matrices may also be used (see, e.g., Schwartz and Dayhoff, eds., 1978, Matrices for Detecting Distance Relationships: Atlas of Protein Sequence and Structure, Washington: National Biomedical Research Foundation)

The BLAST programs evaluate the statistical significance of all high-scoring segment pairs identified, and preferably selects those segments which satisfy a user-specified threshold of significance, such as a user-specified percent homology. Preferably, the statistical significance of a high-scoring segment pair is evaluated using the statistical significance formula of Karlin (see, e.g.,

10

15

Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268).

Equivalent amino acids may be determined either based on their structural homology with the amino acids for which they are substituted, or on results of comparative tests of biological activity between the various polypeptides which may be carried out.

By way of example, there may be mentioned the possibilities of substitutions which may be carried out without resulting in a substantial modification of the biological activity of the corresponding modified polypeptides; the replacements, for example, of leucine with valine or isoleucine, of aspartic acid with glutamic acid, of glutamine with asparagine, of arginine with lysine, and the like, the reverse substitutions naturally being feasible under the same conditions.

The homologous polypeptides also correspond to the polypeptides encoded by the homologous nucleotide sequences as defined above and thus comprise in the present definition the mutated polypeptides or polypeptides corresponding to inter- or intra-species variations which may exist in *Chlamydia*, and which correspond in particular to truncations, substitutions, deletions and/or additions of at least one amino acid residue.

Biologically active fragment of a polypeptide according to the invention will be understood to designate in particular a polypeptide fragment, as defined below, exhibiting at least one of the characteristics of the polypeptides according to the invention, in particular in that it is:

- capable of eliciting an immune response directed against Chlamydia trachomatis; and/or
- capable of being recognized by an antibody specific for a polypeptide according to the 20 invention; and/or
 - capable of binding to a polypeptide or to a nucleotide sequence of *Chlamydia trachomatis*; and/or
 - capable of modulating, regulating, inducing or inhibiting the expression of a gene of *Chlamydia trachomatis* or one of its associated microorganisms, and/or capable of modulating the replication cycle of *Chlamydia trachomatis* or one of its associated microorganisms in the host cell and/or organism; and/or
 - capable of generally exerting an even partial physiological activity, such as for example a structural activity (cellular envelope, ribosome), an enzymatic (metabolic) activity, a transport activity, an activity in the secretion or in the virulence.

A representative polypeptide fragment according to the invention is understood to designate a polypeptide comprising a minimum of 5 amino acids, preferably 10 amino acids or preferably 15 amino acids. It is to be understood that such fragments refer only to portions of polypeptides encoded by ORF2 or ORF1197 that are not currently listed in a publicly available database.

The polypeptide fragments according to the invention may correspond to isolated or

purified fragments which are naturally present in *Chlamydia trachomatis* or which are secreted by *Chlamydia trachomatis*, or may correspond to fragments capable of being obtained by cleaving the said polypeptide with a proteolytic enzyme, such as trypsin or chymotrypsin or collagenase, or with a chemical reagent, such as cyanogen bromide (CNBr) or alternatively by placing the said polypeptide in a highly acidic environment, for example at pH 2.5. Such polypeptide fragments may be equally well prepared by chemical synthesis, using hosts transformed with an expression vector according to the invention containing a nucleic acid allowing the expression of the said fragments, placed under the control of appropriate elements for regulation and/or expression.

«Modified polypeptide» of a polypeptide according to the invention is understood to designate a polypeptide obtained by genetic recombination or by chemical synthesis as will be described below, exhibiting at least one modification in relation to the normal sequence. These modifications may in particular affect amino acids responsible for a specificity or for the efficiency of the activity, or responsible for the structural conformation, for the charge or for the hydrophobicity, and for the capacity for multimerization and for membrane insertion of the polypeptide according to the invention. It is thus possible to create polypeptides with an equivalent, an increased or a reduced activity, and with an equivalent, a narrower or a broader specificity. Among the modified polypeptides, there may be mentioned the polypeptides in which up to 5 amino acids may be modified, truncated at the N- or C-terminal end, or alternatively deleted, or else added.

As is indicated, the modifications of the polypeptide may have in particular the 20 objective:

- of making it capable of modulating, regulating, inhibiting or inducing the expression of a gene of *Chlamydia*, in particular of *Chlamydia trachomatis* and its variants, or one of its associated microorganisms, and/or capable of modulating the replication cycle of *Chlamydia*, in particular of *Chlamydia trachomatis* and its variants, or one of its associated microorganisms, in the host cell and/or organism,
- of allowing its use in methods of biosynthesis or of biodegradation, or its incorporation into vaccine compositions,
- of modifying its bioavailability as a compound for therapeutic use.

The said modified polypeptides may also be used on any cell or microorganism for which the said modified polypeptides will be capable of modulating, regulating, inhibiting or inducing gene expression, or of modulating the growth or the replication cycle of the said cell or of the said microorganism. The methods allowing demonstration of the said modulations on eukaryotic or prokaryotic cells are well known to persons skilled in the art. The said cells or microorganisms will be chosen, in particular, from tumour cells or infectious microorganisms and the said modified polypeptides may be used for the prevention or treatment of pathologies linked to the presence of the

said cells or of the said microorganisms. It is also clearly understood that the nucleotide sequences encoding the said modified polypeptides may be used for the said modulations, for example by the intermediacy of vectors according to the invention and which are described below, so as to prevent or to treat the said pathologies.

The above modified polypeptides may be obtained using combinatory chemistry, in which it is possible to systematically vary portions of the polypeptide before testing them on models, cell cultures or microorganisms for example, so as to select the compounds which are the most active or which exhibit the desired properties.

Chemical synthesis also has the advantage of being able to use:

10

15

20

5

- nonnatural amino acids, or
- nonpeptide bonds.

Accordingly, in order to extend the life of the polypeptides according to the invention, it may be advantageous to use nonnatural amino acids, for example in the D form, or alternatively amino acid analogues, in particular sulphur-containing forms for example.

Finally, the structure of the polypeptides according to the invention, its homologous or modified forms, as well as the corresponding fragments may be integrated into chemical structures of the polypeptide type and the like. Accordingly, it may be advantageous to provide at the N- and C-terminal ends compounds which are not recognized by proteases.

Also forming part of the invention are the nucleotide sequences encoding a polypeptide according to the invention. Described below are ORF nucleotide sequences encoding polypeptides exhibiting particularly preferable characteristics. For each group of preferred ORFs described below, it is to be understood that in addition to the individual ORFs listed, in instances wherein such ORFs are present as part of «combined» ORFs, the «combined» ORFs are also to be included within the preferred group.

More particularly, the subject of the invention is nucleotide sequences, characterized in that they encode a polypeptide of the cellular envelope, preferably of the outer cellular envelope of *Chlamydia trachomatis* or one of its representative fragments, such as for example the predominant proteins of the outer membrane, the adhesion proteins or the proteins entering into the composition of the Chlamydia wall. Among these sequences, the sequences comprising a nucleotide sequence chosen from the following sequences are most preferred:

ORF3; ORF19; ORF51; ORF189; ORF212; ORF213; ORF324; ORF477; ORF478; ORF479; ORF481; ORF482; ORF483; ORF484; ORF486; ORF488; ORF489; ORF490; ORF572; ORF573; ORF742; ORF817; ORF818; ORF820; ORF1035; ORF1036; ORF1037; ORF1038; ORF1070; ORF1071; ORF1073 and one of their representative fragments.

35

The structure of the cytoplasmic membranes and of the wall of bacteria is dependent

on the associated proteins. The structure of the cytoplasmic membrane makes it impermeable to water, to water-soluble substances and to small-sized molecules (ions, small inorganic molecules, peptides or proteins). To enter into or to interfere with a cell or a bacterium, a ligand must establish a special relationship with a protein anchored in the cytoplasmic membrane (the receptor). These proteins which are anchored on the membrane play an important role in metabolism since they control the exchanges in the bacterium. These exchanges apply to molecules of interest for the bacterium (small molecules such as sugars and small peptides) as well as undesirable molecules for the bacterium such as antibiotics or heavy metals.

The double lipid layer structure of the membrane requires the proteins which are inserted therein to have hydrophobic domains of about twenty amino acids forming an alpha helix. Predominantly hydrophobic and potentially transmembrane regions may be predicted from the primary sequence of the proteins, itself deduced from the nucleotide sequence. The presence of one or more putative transmembrane domains raises the possibility for a protein to be associated with the cytoplasmic membrane and to be able to play an important metabolic role therein or alternatively for the protein thus exposed to be able to exhibit potentially protective epitopes.

If the proteins inserted into the membrane exhibit several transmembrane domains capable of interacting with one another via electrostatic bonds, it then becomes possible for these proteins to form pores which go across the membrane which becomes permeable for a number of substances. It should be noted that proteins which do not have transmembrane domains may also be anchored by the intermediacy of fatty acids in the cytoplasmic membrane, it being possible for the breaking of the bond between the protein and its anchor in some cases to be responsible for the release of the peptide outside the bacterium.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* transmembrane polypeptide or one of its representative fragments, having between 1 and 3 transmembrane domains and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF2; ORF3; ORF5; ORF8; ORF9; ORF10; ORF11; ORF12; ORF17; ORF21; ORF26; ORF27; ORF28; ORF29; ORF30; ORF31; ORF33; ORF35; ORF37; ORF39; ORF40; ORF41; ORF42; ORF43; ORF44; ORF45; ORF46; ORF47; ORF48; ORF49; ORF52; ORF53; ORF55; ORF56; ORF58; ORF65; ORF66; ORF68; ORF70; ORF74; ORF75; ORF76; ORF78; ORF79; ORF81; ORF82; ORF83; ORF86; ORF91; ORF92; ORF94; ORF97; ORF100; ORF102; ORF103; ORF105; ORF106; ORF107; ORF109; ORF110; ORF111; ORF112; ORF113; ORF114; ORF115; ORF116; ORF117; ORF120; ORF122; ORF123; ORF130; ORF134; ORF135; ORF137; ORF140; ORF141; ORF143; ORF144; ORF145; ORF147; ORF148; ORF149; ORF150; ORF151; ORF155; ORF156; ORF162; ORF163; ORF164; ORF165; ORF166; ORF166; ORF167; ORF168; ORF169; ORF170; ORF171;

WO 99/28475 PCT/IB98/01939

23

```
ORF173; ORF175; ORF176; ORF187; ORF181; ORF183; ORF184; ORF186; ORF187; ORF188;
    ORF190; ORF191; ORF192; ORF194; ORF195; ORF196; ORF197; ORF198; ORF199; ORF201;
    ORF202; ORF204; ORF206; ORF207; ORF209; ORF212; ORF213; ORF217; ORF219; ORF220;
    ORF221; ORF222; ORF223; ORF224; ORF225; ORF227; ORF228; ORF231; ORF232; ORF234;
 5 ORF236; ORF243; ORF244; ORF245; ORF247; ORF248; ORF249; ORF252; ORF254;
    ORF257; ORF260; ORF261; ORF263; ORF265; ORF266; ORF267; ORF270; ORF271; ORF272;
    ORF274; ORF276; ORF277; ORF278; ORF279; ORF282; ORF283; ORF284; ORF285; ORF287;
    ORF289; ORF290; ORF291; ORF294; ORF298; ORF305; ORF306; ORF310; ORF311; ORF313;
    ORF315; ORF316; ORF319; ORF320; ORF322; ORF323; ORF325; ORF326; ORF327; ORF328;
10 ORF330; ORF331; ORF332; ORF333; ORF334; ORF335; ORF336; ORF338; ORF339; ORF340;
    ORF341; ORF344; ORF345; ORF348; ORF349; ORF350; ORF351; ORF352; ORF353; ORF356;
    ORF357; ORF358; ORF361; ORF362; ORF366; ORF367; ORF368; ORF370; ORF372; ORF373;
    ORF375; ORF377; ORF378; ORF380; ORF382; ORF383; ORF384; ORF385; ORF387;
    ORF389; ORF390; ORF391; ORF393; ORF396; ORF398; ORF399; ORF403; ORF404; ORF406;
15 ORF407; ORF413; ORF414; ORF417; ORF418; ORF420; ORF421; ORF424; ORF426; ORF427;
    ORF428; ORF430; ORF433; ORF434; ORF435; ORF436; ORF437; ORF440; ORF443; ORF446;
    ORF448; ORF450; ORF451; ORF454; ORF455; ORF457; ORF458; ORF459; ORF463; ORF464;
    ORF466; ORF467; ORF468; ORF469; ORF470; ORF473; ORF474; ORF475; ORF476; ORF477;
    ORF479; ORF480; ORF481; ORF483; ORF484; ORF485; ORF486; ORF487; ORF488; ORF491;
20 ORF493; ORF496; ORF497; ORF498; ORF500; ORF501; ORF503; ORF504; ORF508; ORF512;
    ORF513; ORF514; ORF519; ORF521; ORF523; ORF524; ORF526; ORF527; ORF529; ORF530;
    ORF531; ORF532; ORF534; ORF536; ORF537; ORF538; ORF540; ORF541; ORF542; ORF543;
    ORF544; ORF545; ORF546; ORF547; ORF551; ORF552; ORF553; ORF555; ORF558; ORF559;
    ORF560; ORF561; ORF562; ORF566; ORF567; ORF568; ORF569; ORF571; ORF572; ORF574;
   ORF575; ORF576; ORF580; ORF582; ORF585; ORF587; ORF589; ORF592; ORF593; ORF595;
    ORF596; ORF597; ORF599; ORF601; ORF602; ORF603; ORF604; ORF608; ORF609; ORF610;
    ORF611; ORF615; ORF616; ORF617; ORF618; ORF621; ORF622; ORF623; ORF624; ORF625;
    ORF628; ORF632; ORF633; ORF634; ORF635; ORF637; ORF638; ORF640; ORF641; ORF643;
    ORF646; ORF648; ORF651; ORF652; ORF653; ORF654; ORF655; ORF658; ORF664;
   ORF665; ORF666; ORF668; ORF669; ORF670; ORF671; ORF672; ORF673; ORF674; ORF676;
    ORF677; ORF678; ORF680; ORF682; ORF683; ORF684; ORF686; ORF688; ORF689; ORF690;
    ORF691; ORF692; ORF693; ORF695; ORF696; ORF698; ORF701; ORF703; ORF704; ORF705;
    ORF706; ORF707; ORF709; ORF710; ORF711; ORF712; ORF713; ORF714; ORF715; ORF717;
    ORF718; ORF720; ORF721; ORF722; ORF724; ORF726; ORF728; ORF729; ORF730; ORF731;
35 ORF732; ORF734; ORF737; ORF738; ORF739; ORF740; ORF742; ORF743; ORF744;
```

ORF745; ORF746; ORF748; ORF750; ORF751; ORF752; ORF753; ORF754; ORF755; ORF757; ORF758; ORF759; ORF760; ORF764; ORF766; ORF768; ORF769; ORF771; ORF772; ORF773; ORF774; ORF775; ORF776; ORF777; ORF778; ORF779; ORF780; ORF781; ORF782; ORF783; ORF786; ORF787; ORF788; ORF789; ORF790; ORF793; ORF798; ORF800; ORF802; ORF803; 5 ORF806; ORF808; ORF809; ORF810; ORF811; ORF813; ORF814; ORF817; ORF820; ORF822; ORF824; ORF825; ORF827; ORF828; ORF829; ORF830; ORF833; ORF834; ORF835; ORF837; ORF838; ORF839; ORF840; ORF841; ORF842; ORF843; ORF845; ORF848; ORF849; ORF850; ORF851; ORF852; ORF854; ORF855; ORF856; ORF857; ORF859; ORF860; ORF862; ORF863; ORF864; ORF866; ORF869; ORF872; ORF873; ORF874; ORF878; ORF879; ORF880; ORF881; 10 ORF883; ORF884; ORF885; ORF886; ORF887; ORF892; ORF893; ORF894; ORF895; ORF897; ORF899; ORF900; ORF901; ORF904; ORF906; ORF909; ORF910; ORF912; ORF914; ORF917; ORF920; ORF921; ORF922; ORF923; ORF924; ORF925; ORF926; ORF927; ORF930; ORF933; ORF934; ORF935; ORF936; ORF937; ORF940; ORF941; ORF942; ORF943; ORF944; ORF945; ORF947; ORF948; ORF951; ORF952; ORF953; ORF954; ORF955; ORF956; ORF957; ORF958; ORF960; ORF961; ORF962; ORF963; ORF964; ORF966; ORF967; ORF969; ORF970; ORF971; ORF973; ORF974; ORF979; ORF980; ORF981; ORF982; ORF984; ORF988; ORF989; ORF990; ORF991; ORF995; ORF996; ORF999; ORF1001; ORF1003; ORF1004; ORF1005; ORF1006; ORF1007; ORF1009; ORF1010; ORF1011; ORF1012; ORF1013; ORF1014; ORF1016; ORF1017; ORF1018; ORF1020; ORF1021; ORF1025; ORF1026; ORF1027; ORF1029; ORF1030; ORF1031; ORF1035; ORF1036; ORF1037; ORF1038; ORF1039; ORF1040; ORF1044; ORF1045; ORF1047; ORF1048; ORF1050; ORF1051; ORF1052; ORF1053; ORF1055; ORF1056; ORF1057; ORF1058; ORF1061; ORF1062; ORF1063; ORF1064; ORF1065; ORF1066; ORF1068; ORF1069; ORF1072; ORF1074; ORF1076 and one of their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* transmembrane polypeptide or one of its representative fragments, having between 4 and 6 transmembrane domains and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF7; ORF14; ORF16; ORF32; ORF34; ORF36; ORF38; ORF50; ORF57; ORF59; ORF61; ORF62; ORF63; ORF64; ORF67; ORF69; ORF72; ORF77; ORF80; ORF84; ORF87; ORF93; ORF95; ORF99; ORF108; ORF119; ORF125; ORF126; ORF129; ORF131; ORF136; ORF139; ORF146; ORF152; ORF154; ORF160; ORF161; ORF172; ORF179; ORF182; ORF185; ORF200; ORF203; ORF205; ORF239; ORF242; ORF250; ORF253; ORF256; ORF259; ORF262; ORF268; ORF275; ORF281; ORF286; ORF288; ORF292; ORF295; ORF296; ORF297; ORF299; ORF300; ORF308; ORF314; ORF317; ORF318; ORF324; ORF342; ORF343; ORF355; ORF360; ORF374; ORF376; ORF386; ORF388; ORF392; ORF394; ORF395; ORF405; ORF405; ORF411; ORF415; ORF416;

ORF422; ORF423; ORF429; ORF432; ORF441; ORF442; ORF444; ORF449; ORF452; ORF456; ORF460; ORF461; ORF465; ORF471; ORF472; ORF482; ORF489; ORF492; ORF494; ORF495; ORF502; ORF505; ORF506; ORF509; ORF516; ORF517; ORF520; ORF525; ORF533; ORF539; ORF549; ORF554; ORF557; ORF563; ORF570; ORF573; ORF581; ORF590; ORF591; ORF600; ORF607; ORF612; ORF613; ORF620; ORF626; ORF629; ORF630; ORF639; ORF644; ORF647; ORF656; ORF659; ORF661; ORF685; ORF687; ORF699; ORF700; ORF708; ORF716; ORF719; ORF725; ORF747; ORF749; ORF756; ORF765; ORF767; ORF794; ORF796; ORF797; ORF799; ORF801; ORF807; ORF821; ORF823; ORF826; ORF847; ORF853; ORF861; ORF870; ORF871; ORF875; ORF882; ORF888; ORF889; ORF898; ORF902; ORF903; ORF911; ORF916; ORF931; ORF939; ORF975; ORF976; ORF978; ORF983; ORF986; ORF987; ORF992; ORF993; ORF1000; ORF1002; ORF1008; ORF1019; ORF1022; ORF1032; ORF1034; ORF1046; ORF1054; ORF1060; ORF1071 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* transmembrane polypeptide or one of its representative fragments, having at least 7 transmembrane domains and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF4; ORF6; ORF13; ORF20; ORF51; ORF71; ORF88; ORF118; ORF128; ORF132; ORF133; ORF158; ORF159; ORF174; ORF180; ORF189; ORF210; ORF211; ORF214; ORF215; ORF226; ORF229; ORF233; ORF235; ORF240; ORF246; ORF251; ORF255; ORF273; ORF354; ORF364; ORF369; ORF371; ORF397; ORF401; ORF409; ORF412; ORF419; ORF439; ORF453; ORF462; ORF490; ORF510; ORF511; ORF518; ORF535; ORF548; ORF550; ORF564; ORF565; ORF578; ORF579; ORF614; ORF631; ORF636; ORF650; ORF662; ORF667; ORF679; ORF681; ORF702; ORF727; ORF741; ORF763; ORF791; ORF792; ORF815; ORF816; ORF832; ORF846; ORF858; ORF865; ORF867; ORF868; ORF877; ORF891; ORF896; ORF907; ORF908; ORF918; ORF919;

ORF932; ORF959; ORF977; ORF994; ORF998; ORF1024; ORF1028; ORF1042; ORF1067; ORF1070; ORF1073 and one of their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* surface exposed polypeptide (e.g., an outer membrane protein) or one of its representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences:

ORF 2, ORF 3, ORF 21, ORF 22, ORF 23, ORF 53, ORF 77, ORF 187, ORF 203, ORF 383, ORF

ORF 2, ORF 3, ORF 21, ORF 22, ORF 23, ORF 53, ORF 77, ORF 187, ORF 203, ORF 383, ORF 477, ORF 478, ORF 479, ORF 481, ORF 482, ORF 483, ORF 484, ORF 485, ORF 486, ORF 487, ORF 488, ORF 489, ORF 490, ORF 571, ORF 572, ORF 573, ORF 593, ORF 670, ORF 693, ORF 742, ORF 749, ORF 801, ORF 817, ORF 818, ORF 819, ORF 820, ORF 851, ORF 902, ORF 923, ORF 1035, ORF 1036, ORF 1037, ORF 1038, ORF 1069, ORF 1070, ORF 1071, ORF 1073, ORF

30

35

1076, ORF 1095, ORF 1096, ORF 1141, ORF 1181, and their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* lipoprotein or one of its representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences:

ORF 29, ORF 42, ORF 66, ORF 72, ORF 76, ORF 78, ORF 148, ORF 154, ORF 180, ORF 182, ORF 184, ORF 187, ORF 200, ORF 242, ORF 245, ORF 250, ORF 253, ORF 272, ORF 274, ORF 275, ORF 308, ORF 350, ORF 362, ORF 383, ORF 394, ORF 396, ORF 399,

ORF 422, ORF 488, ORF 535, ORF 568, ORF 573, ORF 578, ORF 593, ORF 607, ORF 625, ORF 662, ORF 669, ORF 688, ORF 690, ORF 716, ORF 773, ORF 778, ORF 781, ORF 783, ORF 788, ORF 817, ORF 848, ORF 851, ORF 853, ORF 857, ORF 875, ORF 877, ORF 886, ORF 898, ORF 902, ORF 923, ORF 938, ORF 976, ORF 978, ORF 990, ORF 1005, ORF 1021, ORF 1035, ORF 1069, ORF 1083, ORF 1088, ORF 1089, ORF 1091, ORF 1092, ORF 1095, ORF 1096, ORF 1100, ORF 1105, ORF 1108, ORF 1117, ORF 1120, ORF 1121, ORF 1124, ORF 1128, ORF 1133, ORF 1135, ORF 1139, ORF 1140, ORF 1157, ORF 1159, ORF 1163, ORF 1165, ORF 1167, ORF 1168, ORF 1169, ORF 1171, ORF 1173, ORF 1174, ORF 1177, ORF 1180, ORF 1181, ORF 1186, ORF 1194, ORF 1197, and their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide involved in lipopolysaccharide (LPS) biosynthesis, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences: ORF 17, ORF 201, ORF 691, ORF 807, ORF 936, ORF 983, ORF 1019, ORF 1077 and one of their representative fragments.

Preferably the invention relates to additional LPS-related nucleotide sequences according to the invention, characterized in that they encode:

- (a) a Chlamydia trachomatis KDO (3-deoxy-D-manno-octulosonic acid)-related polypeptide or one of its representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences: ORF 41, ORF 242, ORF 269, ORF 772, and one of their representative fragments;
- (b) a Chlamydia trachomatis phosphomannomutase-related polypeptide or one of its representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequence: ORF 139, and one of its representative fragments;
 - (c) a Chlamydia trachomatis phosphoglucomutase-related polypeptide or one of its representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequence: ORF 567, and one of its representative fragments; and
 - (d) a Chlamydia trachomatis lipid A component-related polypeptide or one of its

representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences: ORF 4, ORF 933, ORF 934, ORF 935, ORF 1185, and one of their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* Type III or other, non-Type III secreted polypeptides or one of its representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences: ORF 180, ORF 181, ORF 207, ORF 208, ORF 372, ORF 391, ORF 399, ORF 477, ORF 486, ORF 749, ORF 758, ORF 819, ORF 878, ORF 888, ORF 896, ORF 897, ORF 900, ORF 902, ORF 923, ORF 1015, ORF 1018, ORF 1059, ORF 1060, ORF 1069, ORF 1071, ORF 1073, ORF 1076, ORF 1189, and their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide containing RGD (Arg-Gly-Asp) attachment sites or one of its representative fragments:

- 15 (a) RGD-containing proteins that are outer membrane proteins, are more likely to play a role in cell attachment. ORFs that encoded a protein containing an RGD sequence and also were classified as outer membrane proteins are ORF 488, ORF 489, ORF 571, ORF 572, ORF 573 or ORF 716, and its representative fragments.
- (b) The outer membrane of Chlamydia is made of cysteine-rich proteins that form a network of both intra and inter molecular disulfide links. This contributes to the integrity of the membrane since Chlamydia lacks the peptidoglycan layer that other gram-negative bacteria have. Cysteine-rich proteins that have the RGD sequence are also considered to be potential vaccine candidates. Cysteine-rich proteins were defined as proteins that had more than 3.0% cysteine in their primary amino acid sequence, above the mean genomic ORF cysteine content. The corresponding ORF is: ORF 1144 and one of its representative fragments.
- (c) The outer membrane of Chlamydia may also contain small proteins that have cysteines in their N- and C-terminus that may contribute to the network formed by disulfide linkages.
 30 These proteins may be anchored in the outer membrane via their N-terminus and may have their C-terminus exposed, which then can interact with the host cells. Alternatively, these proteins may be anchored in the outer membrane via both N-and C-terminus and may have regions in the middle that may be exposed which can in turn interact with the host cells. ORFs encoding polypeptides that contain cysteines in their first 30 amino acids and also contain an RGD sequence are: ORF 101, ORF 122, ORF 308, ORF 488, ORF 489, ORF 571, ORF 572, ORF 573, ORF 651, ORF 679, ORF 680,

ORF 705, ORF 716, ORF 763, ORF 870, ORF 878, ORF 879, ORF 995, ORF 1028, ORF 1029, ORF 1176, and one of their representative fragments.

(d) RGD-containing ORFs homologous to RGD-containing ORFs from
 5 Chlamydia pneumoniae are:
 ORF 28, ORF 101, ORF 125, ORF 155, ORF 156, ORF 286, ORF 571, ORF 572, ORF 573, ORF
 763, ORF 870, and one of their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* cell wall anchored surface polypeptide or one of its representative fragments, said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences: ORF 662, ORF 681, ORF 1182, ORF 1192, and their representative fragments.

Preferably, the invention relates to the nucleotide sequences according to the 15 invention, characterized in that they encode Chlamydia trachomatis polypeptides not found in Chlamydia pneumoniae (Blastp P>e-10), said nucleotide sequences comprising a nucleotide sequence chosen from the following sequences: ORF 2, ORF 18, ORF 60, ORF 66, ORF 67, ORF 68, ORF 69, ORF 70, ORF 81, ORF 89, ORF 107, ORF 108, ORF 109, ORF 134, ORF 147, ORF 191, ORF 194, ORF 216, ORF 217, ORF 218, ORF 219, ORF 220, ORF 221, ORF 222, ORF 223, ORF 224, ORF 20 225, ORF 228, ORF 235, ORF 257, ORF 276, ORF 277, ORF 278, ORF 279, ORF 280, ORF 281, ORF 282, ORF 283, ORF 284, ORF 285, ORF 289, ORF 291, ORF 298, ORF 313, ORF 314, ORF 315, ORF 316, ORF 334, ORF 335, ORF 336, ORF 337, ORF 338, ORF 339, ORF 340, ORF 381, ORF 393, ORF 413, ORF 418, ORF 419, ORF 420, ORF 421, ORF 422, ORF 423, ORF 436, ORF 460, ORF 475, ORF 476, ORF 480, ORF 485, ORF 487, ORF 491, ORF 492, ORF 493, ORF 494, 25 ORF 496, ORF 500, ORF 504, ORF 514, ORF 527, ORF 559, ORF 569, ORF 570, ORF 575, ORF 580, ORF 582, ORF 593, ORF 598, ORF 632, ORF 640, ORF 651, ORF 671, ORF 690, ORF 694, ORF 698, ORF 710, ORF 722, ORF 723, ORF 724, ORF 770, ORF 771, ORF 782, ORF 783, ORF 784, ORF 790, ORF 795, ORF 798, ORF 805, ORF 810, ORF 817, ORF 829, ORF 830, ORF 864, ORF 866, ORF 876, ORF 887, ORF 892, ORF 899, ORF 913, ORF 921, ORF 933, ORF 938, ORF 30 949, ORF 956, ORF 1010, ORF 1017, ORF 1018, ORF 1027, ORF 1030, ORF 1037, ORF 1038, ORF 1047, ORF 1072, ORF 1074, ORF 1075, ORF 1078, ORF 1079, ORF 1081, ORF 1083, ORF 1084, ORF 1087, ORF 1088, ORF 1089, ORF 1091, ORF 1092, ORF 1094, ORF 1095, ORF 1096, ORF 1098, ORF 1104, ORF 1105, ORF 1106, ORF 1108, ORF 1110, ORF 1114, ORF 1115, ORF 1116, ORF 1117, ORF 1119, ORF 1128, ORF 1132, ORF 1133, ORF 1135, ORF 1136, ORF 1139, ORF 1140, ORF 1141, ORF 1142, ORF 1144, ORF 1148, ORF 1151, ORF 1155, ORF 1157, ORF 1159, 35

ORF 1161, ORF 1162, ORF 1165, ORF 1166, ORF 1167, ORF 1168, ORF 1169, ORF 1171, ORF 1172, ORF 1173, ORF 1174, ORF 1175, ORF 1176, ORF 1177, ORF 1178, ORF 1180, ORF 1181, ORF 1183, ORF 1184, ORF 1186, ORF 1187, ORF 1188, ORF 1192, ORF 1194, ORF 1197, and their representative fragments.

5 Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a Chlamydia trachomatis polypeptide or one of its representative fragments which is involved in the intermediate metabolism, in particular in the metabolism of sugars and/or of cofactors, such as for example triose phosphate isomerase or pyruvate kinase, and in that they comprise a nucleotide sequence chosen from the following sequences: 10 ORF10; ORF44; ORF45; ORF46; ORF47; ORF93; ORF101; ORF102; ORF103; ORF106; ORF107; ORF120; ORF121; ORF130; ORF135; ORF140; ORF143; ORF144; ORF145; ORF158; ORF159; ORF160; ORF161; ORF192; ORF193; ORF196; ORF197; ORF198; ORF199; ORF227; ORF229; ORF236; ORF236; ORF239; ORF243; ORF245; ORF264; ORF265; ORF297; ORF331; ORF333; ORF359; ORF360; ORF374; ORF404; ORF405; ORF405; ORF410; ORF415; ORF415; ORF416; ORF417; ORF432; ORF460; ORF461; ORF462; ORF495; ORF513; ORF515; ORF566; ORF566; ORF566; ORF589; ORF613; ORF645; ORF646; ORF647; ORF652; ORF653; ORF654; ORF672; ORF673; ORF674; ORF682; ORF684; ORF692; ORF700; ORF725; ORF801; ORF802; ORF835; ORF836; ORF837; ORF860; ORF861; ORF862; ORF863; ORF869; ORF869; ORF925; ORF964; ORF983 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the intermediate metabolism of nucleotides or nucleic acids, such as for example CTP synthetase or GMP synthetase, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF142; ORF142; ORF169; ORF256; ORF268; ORF325; ORF352; ORF366; ORF435; ORF444; ORF528; ORF529; ORF530; ORF548; ORF549; ORF601; ORF602; ORF617; ORF619; ORF644; ORF745; ORF971; ORF972; ORF1023 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of nucleic acids, such as for example DNA polymerases or DNA topoisomerases, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF5; ORF12; ORF82; ORF96; ORF97; ORF98; ORF99; ORF100; ORF105; ORF118; ORF136; ORF137; ORF163; ORF190; ORF204; ORF259; ORF260; ORF262; ORF290; ORF300; ORF301; ORF302; ORF387; ORF427; ORF434; ORF441; ORF444; ORF471; ORF595; ORF596; ORF597;

ORF599; ORF600; ORF605; ORF612; ORF624; ORF625; ORF650; ORF657; ORF658; ORF702; ORF703; ORF704; ORF708; ORF719; ORF766; ORF767; ORF775; ORF779; ORF787; ORF788; ORF794; ORF841; ORF842; ORF883; ORF884; ORF907; ORF918; ORF924; ORF928; ORF929; ORF962; ORF962; ORF963; ORF969; ORF970; ORF975; ORF979; ORF995; ORF1031; ORF1032 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of amino acids or polypeptides, such as for example serine hydroxymethyl transferase or the proteins which load amino acids onto transfer RNAs, and in that they comprise a nucleotide sequence chosen from the following sequences: ORF27; ORF41; ORF55; ORF56; ORF57; ORF59; ORF62; ORF63; ORF64; ORF65; ORF119; ORF132; ORF240; ORF241; ORF277; ORF278; ORF279; ORF382; ORF406; ORF428; ORF442; ORF446; ORF447; ORF453; ORF454; ORF541; ORF542; ORF591; ORF608; ORF609; ORF610; ORF618; ORF648; ORF649; ORF660; ORF661; ORF677; ORF717; ORF765; ORF797; ORF871; ORF875; ORF920; ORF922; ORF937; ORF998; ORF1020; ORF1021; ORF1034; ORF1044; ORF1046; ORF1049 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of polypeptides, such as for example protein kinases or proteases, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF21; ORF22; ORF23; ORF24; ORF25; ORF26; ORF75; ORF84; ORF86; ORF92; ORF133;
ORF151; ORF152; ORF157; ORF179; ORF209; ORF307; ORF326; ORF343; ORF344; ORF345;
ORF371; ORF429; ORF519; ORF557; ORF586; ORF587; ORF630; ORF656; ORF706; ORF707;
ORF730; ORF751; ORF752; ORF786; ORF847; ORF885; ORF923; ORF978; ORF1039; ORF1048 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of fatty acids, such as for example succinyl-CoA-synthesizing proteins or phosphatidylserine synthetase, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF4; ORF15; ORF16; ORF141; ORF173; ORF205; ORF205; ORF206; ORF207; ORF208; ORF312; ORF355; ORF415; ORF550; ORF558; ORF560; ORF561; ORF574; ORF577; ORF578; ORF590; ORF614; ORF772; ORF808; ORF809; ORF904; ORF905; ORF905; ORF933; ORF934; ORF934; ORF936 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the synthesis of the wall, such as for example KDO transferase, and the proteins responsible for the attachment of certain sugars onto the exposed proteins, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF87; ORF196; ORF242; ORF269; ORF628; ORF629; ORF634; ORF635; ORF637; ORF638; ORF1019 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the transcription, translation and/or maturation process, such as for example initiation factors, RNA polymerases or certain chaperone proteins, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF112; ORF113; ORF332; ORF212; ORF213; ORF350; ORF362; ORF363; ORF364; ORF407; ORF451; ORF546; ORF643; ORF744; ORF746; ORF833; ORF868; ORF981; ORF982; ORF1003; ORF1011; ORF1042 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* ribosomal polypeptide or one of its representative fragments, such as for example the ribosomal proteins L21, L27 and S10, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF114; ORF115; ORF116; ORF328; ORF361; ORF375; ORF445; ORF543; ORF584; ORF585; ORF743; ORF813; ORF941; ORF942; ORF944; ORF946; ORF947; ORF948; ORF950; ORF951; ORF952; ORF953; ORF954; ORF955; ORF955; ORF957; ORF958; ORF960; ORF961; ORF1040; ORF1041; ORF1043; ORF1063; ORF1064 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* transport polypeptide or one of its representative fragments, such as for example the proteins for transporting amino acids, sugars and certain oligopeptides, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF6; ORF50; ORF51; ORF80; ORF125; ORF126; ORF128; ORF129; ORF215; ORF246; ORF248; ORF249; ORF251; ORF252; ORF253; ORF255; ORF271; ORF275; ORF293; ORF309; ORF323; ORF324; ORF398; ORF401; ORF449; ORF511; ORF512; ORF564; ORF565; ORF667; ORF679; ORF680; ORF711; ORF712; ORF713; ORF714; ORF715; ORF730; ORF731; ORF736; ORF737; ORF738; ORF870; ORF908; ORF919; ORF977; ORF987; ORF988; ORF992; ORF993; ORF994; ORF1028; ORF1029 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the

invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the virulence process, such as for example the proteins analogous to the *Escherichia coli* vacB protein, and in that they comprise a nucleotide sequence chosen from the following sequences:

5 ORF20; ORF815; ORF816; ORF898; ORF1059; ORF1060 and one of their representative fragments.

Preferably, the invention also relates to the nucleotide sequences according to the invention, characterized in that they encode a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the secretory system and/or which is secreted, such as for example proteins homologous to proteins in the secretory system of certain bacteria such as the Salmonellae or the Yersiniae, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF758; ORF888; ORF889; ORF890; ORF891; ORF896; ORF897; ORF898 and one of their representative fragments.

Preferably, the invention also relates to nucleotide sequences according to the invention, characterized in that they encode a polypeptide specific to Chlamydiae or one of its representative fragments, and in that they comprise a nucleotide sequence chosen from the following sequences:

ORF22; ORF29; ORF31; ORF32; ORF34; ORF35; ORF39; ORF40; ORF43; ORF48; ORF49; ORF50; ORF52; ORF53; ORF54; ORF72; ORF77; ORF78; ORF87; ORF90; ORF95; ORF108; ORF110; ORF111; ORF122; ORF123; ORF124; ORF127; ORF138; ORF144; ORF146; ORF153; ORF155; ORF164; ORF166; ORF175; ORF182; ORF184; ORF186; ORF187; ORF188; ORF202; ORF210; ORF247; ORF258; ORF266; ORF267; ORF270; ORF273; ORF274; ORF295; ORF296; ORF305; ORF306; ORF309; ORF318; ORF319; ORF322; ORF326; ORF342; ORF357; ORF376; ORF379; ORF380; ORF388; ORF390; ORF400; ORF431; ORF433; ORF438; ORF443; ORF456; ORF457; ORF458; ORF464; ORF468; ORF470; ORF473; ORF486; ORF489; ORF497; ORF501; ORF503; ORF504; ORF508; ORF512; ORF521; ORF522; ORF523; ORF524; ORF533; ORF535; ORF536; ORF537; ORF538; ORF539; ORF540; ORF554; ORF563; ORF572; ORF579; ORF595; ORF603; ORF604; ORF606; ORF607; ORF615; ORF616; ORF622; ORF641; ORF642; ORF659; ORF668; ORF670; ORF693; ORF695; ORF696; ORF699; ORF703; ORF704; ORF716; ORF726; 30 ORF728; ORF739; ORF742; ORF747; ORF750; ORF751; ORF755; ORF757; ORF759; ORF761; ORF762; ORF763; ORF764; ORF773; ORF780; ORF781; ORF789; ORF800; ORF803; ORF804; ORF818; ORF820; ORF822; ORF823; ORF824; ORF827; ORF828; ORF839; ORF849; ORF850; ORF851; ORF852; ORF855; ORF856; ORF857; ORF858; ORF859; ORF860; ORF861; ORF862; ORF863; ORF865; ORF868; ORF869; ORF870; ORF871; ORF872; ORF873; ORF874; ORF875; ORF877; ORF878; ORF880; ORF882; ORF884; ORF886; ORF893; ORF901; ORF906; ORF910;

10

ORF912; ORF915; ORF916; ORF917; ORF926; ORF929; ORF933; ORF965; ORF967; ORF968; ORF984; ORF986; ORF989; ORF990; ORF996; ORF997; ORF1001; ORF1002; ORF1013; ORF1016; ORF1031; ORF1033; ORF1035; ORF1049; ORF1051; ORF1052; ORF1054; ORF1056; ORF1057; ORF1058; ORF1062; ORF1070; ORF1071; ORF1073 and one of their representative fragments.

Also forming part of the invention are polypeptides encoded by the polynucleotides of the invention, as well as fusion polypeptides comprising such polypeptides. In one embodiment, the polypeptides and fusion polypeptides immunoreact with seropositive serum of an individual infected with *Chlamydia trachomatis*. For example, described below, are polypeptide sequences exhibiting particularly preferable characteristics. For each group of preferred polypeptides described below, it is to be understood that in addition to the individual polypeptides listed, in instances wherein such polypeptides are encoded as part of «combined» ORFs, such «combined» polypeptides are also to be included within the preferred group.

The subject of the invention is also a polypeptide according to the invention, characterized in that it is a polypeptide of the cellular envelope, preferably of the outer cellular envelope, of *Chlamydia trachomatis* or one of its representative fragments. According to the invention, the said polypeptide is preferably chosen from the polypeptides having the following sequences:

SEQ ID No. 3; SEQ ID No. 19; SEQ ID No. 51; SEQ ID No. 189; SEQ ID No. 212; SEQ ID No. 213; 20 SEQ ID No. 324; SEQ ID No. 477; SEQ ID No. 478; SEQ ID No. 479; SEQ ID No. 481; SEQ ID No. 482; SEQ ID No. 483; SEQ ID No. 484; SEQ ID No. 486; SEQ ID No. 488; SEQ ID No. 489; SEQ ID No. 490; SEQ ID No. 572; SEQ ID No. 573; SEQ ID No. 742; SEQ ID No. 817; SEQ ID No. 818; SEQ ID No. 820; SEQ ID No. 1035; SEQ ID No. 1036; SEQ ID No. 1037; SEQ ID No. 1038; SEQ ID No. 1070; SEQ ID No. 1071; SEQ ID No. 1073 and 25 one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* transmembrane polypeptide or one of its representative fragments, having between 1 and 3 transmembrane domains, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 2; SEQ ID No. 3; SEQ ID No. 5; SEQ ID No. 8; SEQ ID No. 9; SEQ ID No. 10; SEQ ID No. 11; SEQ ID No. 12; SEQ ID No. 17; SEQ ID No. 21; SEQ ID No. 26; SEQ ID No. 27; SEQ ID No. 28; SEQ ID No. 29; SEQ ID No. 30; SEQ ID No. 31; SEQ ID No. 33; SEQ ID No. 35; SEQ ID No. 37; SEQ ID No. 39; SEQ ID No. 40; SEQ ID No. 41; SEQ ID No. 42; SEQ ID No. 43; SEQ ID No. 44; SEQ ID No. 45; SEQ ID No. 46; SEQ ID No. 47; SEQ ID No. 48; SEQ ID No. 49;
SEQ ID No. 52; SEQ ID No. 53; SEQ ID No. 55; SEQ ID No. 56; SEQ ID No. 58; SEQ ID No. 65;

SEQ ID No. 66; SEQ ID No. 68; SEQ ID No. 70; SEQ ID No. 74; SEQ ID No. 75; SEQ ID No. 76; SEQ ID No. 78; SEQ ID No. 79; SEQ ID No. 81; SEQ ID No. 82; SEQ ID No. 83; SEQ ID No. 86; SEQ ID No. 91; SEQ ID No. 92; SEQ ID No. 94; SEQ ID No. 97; SEQ ID No. 100; SEQ ID No. 102; SEQ ID No. 109; SEQ ID No. 107; SEQ ID No. 106; SEQ ID No. 105; SEQ ID No. 103; SEQ ID No. 114; SEQ ID No. 113; SEQ ID No. 111; SEQ ID No. 112; 5 SEQ ID No. 110; SEQ ID No. 122; SEQ ID No. 120; SEQ ID No. 117; SEQ ID No. 116; SEQ ID No. 115; SEQ ID No. 137; SEQ ID No. 135; SEQ ID No. 134; SEQ ID No. 130; SEQ ID No. 123; SEQ ID No. 145; SEQ ID No. 144; SEQ ID No. 143; SEQ ID No. 141; SEQ ID No. 140; SEQ ID No. 151; SEQ ID No. 150; SEQ ID No. 149; SEQ ID No. 148; SEO ID No. 147; SEQ ID No. 164; SEQ ID No. 162; SEQ ID No. 163; SEQ ID No. 156; SEQ ID No. 155; SEQ ID No. 169; SEQ ID No. 167; SEQ ID No. 168; SEQ ID No. 166; SEQ ID No. 165; SEQ ID No. 176; SEQ ID No. 175; SEQ ID No. 173; SEQ ID No. 171; SEQ ID No. 170; SEQ ID No. 186; SEQ ID No. 184; SEQ ID No. 183; SEQ ID No. 181; SEQ ID No. 177; SEQ ID No. 192; SEQ ID No. 191; SEQ ID No. 190; SEQ ID No. 188; SEQ ID No. 187; SEQ ID No. 198; SEQ ID No. 197; SEQ ID No. 196; SEQ ID No. 195; SEQ ID No. 194; 15 SEQ ID No. 206; SEQ ID No. 204; SEQ ID No. 202; SEQ ID No. 201; SEQ ID No. 199; SEQ ID No. 217; SEQ ID No. 213; SEQ ID No. 212; SEQ ID No. 209; SEQ ID No. 207; SEQ ID No. 223; SEQ ID No. 221; SEQ ID No. 222; SEQ ID No. 220; SEQ ID No. 219; SEQ ID No. 231; SEQ ID No. 228; SEQ ID No. 227; SEQ ID No. 225; SEQ ID No. 224; SEQ ID No. 243; SEQ ID No. 237; SEQ ID No. 236; SEQ ID No. 234; SEQ ID No. 232; SEQ ID No. 249; SEQ ID No. 248; SEQ ID No. 247; SEQ ID No. 245; SEQ ID No. 244; SEQ ID No. 261; SEQ ID No. 260; SEQ ID No. 254; SEQ ID No. 257; SEQ ID No. 252; SEQ ID No. 270; SEQ ID No. 266; SEQ ID No. 267; SEQ ID No. 265; SEQ ID No. 263; SEQ ID No. 277; SEQ ID No. 276; SEQ ID No. 274; SEQ ID No. 272; SEQ ID No. 271; SEQ ID No. 284; SEQ ID No. 283; SEQ ID No. 282; SEQ ID No. 279; SEQ ID No. 278; 25 SEQ ID No. 291; SEQ ID No. 289; SEQ ID No. 290; SEQ ID No. 287; SEQ ID No. 285; SEQ ID No. 310; SEQ ID No. 306; SEQ ID No. 298; SEQ ID No. 305; SEQ ID No. 294; SEQ ID No. 319; SEQ ID No. 316; SEQ ID No. 315; SEQ ID No. 313; SEQ ID No. 311; SEQ ID No. 326; SEQ ID No. 323; SEQ ID No. 325; SEO ID No. 322; SEQ ID No. 320; SEQ ID No. 331; SEQ ID No. 332; SEQ ID No. 330; SEQ ID No. 328; SEQ ID No. 327; SEQ ID No. 336; SEQ ID No. 338; SEQ ID No. 335; SEQ ID No. 334; SEQ ID No. 333; SEQ ID No. 345; SEQ ID No. 344; SEQ ID No. 341; SEQ ID No. 340; SEQ ID No. 339; SEQ ID No. 351; SEQ ID No. 352; SEQ ID No. 350; SEQ ID No. 349; SEO ID No. 348; SEQ ID No. 361; SEQ ID No. 358; SEQ ID No. 357; SEQ ID No. 356; SEQ ID No. 353; SEQ ID No. 370; SEQ ID No. 368; SEQ ID No. 367; SEQ ID No. 366; SEQ ID No. 362;

	SEQ ID No. 372;	SEQ ID No. 373;	SEQ ID No. 375;	SEQ ID No. 377;	SEQ ID No. 378;
	SEQ ID No. 379;	SEQ ID No. 380;	SEQ ID No. 382;	SEQ ID No. 383;	SEQ ID No. 384;
	SEQ ID No. 385;	SEQ ID No. 387;	SEQ ID No. 389;	SEQ ID No. 390;	SEQ ID No. 391;
	SEQ ID No. 393;	SEQ ID No. 396;	SEQ ID No. 398;	SEQ ID No. 399;	SEQ ID No. 403;
5	SEQ ID No. 404;	SEQ ID No. 406;	SEQ ID No. 407;	SEQ ID No. 413;	SEQ ID No. 414;
	SEQ ID No. 417;	SEQ ID No. 418;	SEQ ID No. 420;	SEQ ID No. 421;	SEQ ID No. 424;
	SEQ ID No. 426;	SEQ ID No. 427;	SEQ ID No. 428;	SEQ ID No. 430;	SEQ ID No. 433;
	SEQ ID No. 434;	SEQ ID No. 435;	SEQ ID No. 436;	SEQ ID No. 437;	SEQ ID No. 440;
	SEQ ID No. 443;	SEQ ID No. 446;	SEQ ID No. 448;	SEQ ID No. 450;	SEQ ID No. 451;
10	SEQ ID No. 454;	SEQ ID No. 455;	SEQ ID No. 457;	SEQ ID No. 458;	SEQ ID No. 459;
	SEQ ID No. 463;	SEQ ID No. 464;	SEQ ID No. 466;	SEQ ID No. 467;	SEQ ID No. 468;
	SEQ ID No. 469;	SEQ ID No. 470;	SEQ ID No. 473;	SEQ ID No. 474;	SEQ ID No. 475;
	SEQ ID No. 476;	SEQ ID No. 477;	SEQ ID No. 479;	SEQ ID No. 480;	SEQ ID No. 481;
	SEQ ID No. 483;	SEQ ID No. 484;	SEQ ID No. 485;	SEQ ID No. 486;	SEQ ID No. 487;
15	SEQ ID No. 488;	SEQ ID No. 491;	SEQ ID No. 493;	SEQ ID No. 496;	SEQ ID No. 497;
	SEQ ID No. 498;	SEQ ID No. 500;	SEQ ID No. 501;	SEQ ID No. 503;	SEQ ID No. 504;
	SEQ ID No. 508;	SEQ ID No. 512;	SEQ ID No. 513;	SEQ ID No. 514;	SEQ ID No. 519;
	SEQ ID No. 521;	SEQ ID No. 523;	SEQ ID No. 524;	SEQ ID No. 526;	SEQ ID No. 527;
	SEQ ID No. 529;	SEQ ID No. 530;	SEQ ID No. 531;	SEQ ID No. 532;	SEQ ID No. 534;
20	SEQ ID No. 536;	SEQ ID No. 537;	SEQ ID No. 538;	SEQ ID No. 540;	SEQ ID No. 541;
	SEQ ID No. 542;	SEQ ID No. 543;	SEQ ID No. 544;	SEQ ID No. 545;	SEQ ID No. 546;
	SEQ ID No. 547;	SEQ ID No. 551;	SEQ ID No. 552;	SEQ ID No. 553;	SEQ ID No. 555;
	SEQ ID No. 558;	SEQ ID No. 559;	SEQ ID No. 560;	SEQ ID No. 561;	SEQ ID No. 562;
	SEQ ID No. 566;	SEQ ID No. 567;	SEQ ID No. 568;	SEQ ID No. 569;	SEQ ID No. 571;
25	SEQ ID No. 572;	SEQ ID No. 574;	SEQ ID No. 575;	SEQ ID No. 576;	SEQ ID No. 580;
	SEQ ID No. 582;	SEQ ID No. 585;	SEQ ID No. 587;	SEQ ID No. 589;	SEQ ID No. 592;
	SEQ ID No. 593;	SEQ ID No. 595;	SEQ ID No. 596;	SEQ ID No. 597;	SEQ ID No. 599;
	SEQ ID No. 601;	SEQ ID No. 602;	SEQ ID No. 603;	SEQ ID No. 604;	SEQ ID No. 608;
	SEQ ID No. 609;	SEQ ID No. 610;	SEQ ID No. 611;	SEQ ID No. 615;	SEQ ID No. 616;
30	SEQ ID No. 617;	SEQ ID No. 618;	SEQ ID No. 621;	SEQ ID No. 622;	SEQ ID No. 623;
	SEQ ID No. 624;	SEQ ID No. 625;	SEQ ID No. 628;	SEQ ID No. 632;	SEQ ID No. 633;
	SEQ ID No. 634;	SEQ ID No. 635;	SEQ ID No. 637;	SEQ ID No. 638;	SEQ ID No. 640;
	SEQ ID No. 641;	SEQ ID No. 643;	SEQ ID No. 646;	SEQ ID No. 648;	SEQ ID No. 649;
	SEQ ID No. 651;	SEQ ID No. 652;	SEQ ID No. 653;	SEQ ID No. 654;	SEQ ID No. 655;
35	SEQ ID No. 658;	SEQ ID No. 664;	SEQ ID No. 665;	SEQ ID No. 666;	SEQ ID No. 668;

	SEQ ID No. 669;	SEQ ID No. 670;	SEQ ID No. 671;	SEQ ID No. 672;	SEQ ID No. 673;
	SEQ ID No. 674;	SEQ ID No. 676;	SEQ ID No. 677;	SEQ ID No. 678;	SEQ ID No. 680;
	SEQ ID No. 682;	SEQ ID No. 683;	SEQ ID No. 684;	SEQ ID No. 686;	SEQ ID No. 688;
	SEQ ID No. 689;	SEQ ID No. 690;	SEQ ID No. 691;	SEQ ID No. 692;	SEQ ID No. 693;
5	SEQ ID No. 695;	SEQ ID No. 696;	SEQ ID No. 698;	SEQ ID No. 701;	SEQ ID No. 703;
	SEQ ID No. 704;	SEQ ID No. 705;	SEQ ID No. 706;	SEQ ID No. 707;	SEQ ID No. 709;
	SEQ ID No. 710;	SEQ ID No. 711;	SEQ ID No. 712;	SEQ ID No. 713;	SEQ ID No. 714;
	SEQ ID No. 715;	SEQ ID No. 717;	SEQ ID No. 718;	SEQ ID No. 720;	SEQ ID No. 721;
	SEQ ID No. 722;	SEQ ID No. 724;	SEQ ID No. 726;	SEQ ID No. 728;	SEQ ID No. 729;
10	SEQ ID No. 730;	SEQ ID No. 731;	SEQ ID No. 732;	SEQ ID No. 733;	SEQ ID No. 734;
	SEQ ID No. 737;	SEQ ID No. 738;	SEQ ID No. 739;	SEQ ID No. 740;	SEQ ID No. 742;
	SEQ ID No. 743;	SEQ ID No. 744;	SEQ ID No. 745;	SEQ ID No. 746;	SEQ ID No. 748;
	SEQ ID No. 750;	SEQ ID No. 751;	SEQ ID No. 752;	SEQ ID No. 753;	SEQ ID No. 754;
	SEQ ID No. 755;	SEQ ID No. 757;	SEQ ID No. 758;	SEQ ID No. 759;	SEQ ID No. 760;
15	SEQ ID No. 764;	SEQ ID No. 766;	SEQ ID No. 768;	SEQ ID No. 769;	SEQ ID No. 771;
	SEQ ID No. 772;	SEQ ID No. 773;	SEQ ID No. 774;	SEQ ID No. 775;	SEQ ID No. 776;
	SEQ ID No. 777;	SEQ ID No. 778;	SEQ ID No. 779;	SEQ ID No. 780;	SEQ ID No. 781;
	SEQ ID No. 782;	SEQ ID No. 783;	SEQ ID No. 786;	SEQ ID No. 787;	SEQ ID No. 788;
	SEQ ID No. 789;	SEQ ID No. 790;	SEQ ID No. 793;	SEQ ID No. 798;	SEQ ID No. 800;
20		SEQ ID No. 803;	SEQ ID No. 806;	SEQ ID No. 808;	SEQ ID No. 809;
	SEQ ID No. 810;	SEQ ID No. 811;	SEQ ID No. 813;	SEQ ID No. 814;	SEQ ID No. 817;
	SEQ ID No. 820;	SEQ ID No. 822;	SEQ ID No. 824;	SEQ ID No. 825;	SEQ ID No. 827;
	SEQ ID No. 828;	SEQ ID No. 829;	SEQ ID No. 830;	SEQ ID No. 833;	SEQ ID No. 834;
	SEQ ID No. 835;	SEQ ID No. 837;	SEQ ID No. 838;	SEQ ID No. 839;	SEQ ID No. 840;
25	SEQ ID No. 841;	SEQ ID No. 842;	SEQ ID No. 843;	SEQ ID No. 845;	SEQ ID No. 848;
	SEQ ID No. 849;	SEQ ID No. 850;	SEQ ID No. 851;	SEQ ID No. 852;	SEQ ID No. 854;
	SEQ ID No. 855;	SEQ ID No. 856;	SEQ ID No. 857;	SEQ ID No. 859;	SEQ ID No. 860;
	SEQ ID No. 862;	SEQ ID No. 863;	SEQ ID No. 864;	SEQ ID No. 866;	SEQ ID No. 869;
	SEQ ID No. 872;	SEQ ID No. 873;	SEQ ID No. 874;	SEQ ID No. 878;	SEQ ID No. 879;
30	SEQ ID No. 880;	SEQ ID No. 881;	SEQ ID No. 883;	SEQ ID No. 884;	SEQ ID No. 885;
	SEQ ID No. 886;	SEQ ID No. 887;	SEQ ID No. 892;	SEQ ID No. 893;	SEQ ID No. 894;
	SEQ ID No. 895;	SEQ ID No. 897;	SEQ ID No. 899;	SEQ ID No. 900;	SEQ ID No. 901;
	SEQ ID No. 904;	SEQ ID No. 906;	SEQ ID No. 909;	SEQ ID No. 910;	SEQ ID No. 912;
	SEQ ID No. 914;	SEQ ID No. 917;	SEQ ID No. 920;	SEQ ID No. 921;	SEQ ID No. 922;
3.	5 SEQ ID No. 923;	SEQ ID No. 924;	SEQ ID No. 925;	SEQ ID No. 926;	SEQ ID No. 927;

```
SEQ ID No. 930;
                                         SEQ ID No. 934;
                       SEQ ID No. 933;
                                                           SEQ ID No. 935;
                                                                              SEQ ID No. 936;
    SEQ ID No. 937;
                       SEQ ID No. 940;
                                         SEQ ID No. 941;
                                                           SEQ ID No. 942;
                                                                              SEQ ID No. 943;
    SEQ ID No. 944;
                       SEQ ID No. 945;
                                         SEQ ID No. 947;
                                                           SEQ ID No. 948;
                                                                              SEQ ID No. 951;
    SEQ ID No. 952;
                       SEQ ID No. 953;
                                         SEQ ID No. 954;
                                                           SEQ ID No. 955;
                                                                              SEQ ID No. 956;
 5 SEQ ID No. 957;
                       SEQ ID No. 958;
                                         SEQ ID No. 960;
                                                           SEQ ID No. 961;
                                                                              SEQ ID No. 962;
    SEQ ID No. 963;
                       SEQ ID No. 964;
                                         SEQ ID No. 966;
                                                           SEQ ID No. 967;
                                                                              SEQ ID No. 969;
    SEQ ID No. 970;
                       SEQ ID No. 971;
                                         SEQ ID No. 973;
                                                           SEQ ID No. 974;
                                                                              SEQ ID No. 979;
    SEQ ID No. 980;
                       SEQ ID No. 981;
                                         SEQ ID No. 982;
                                                           SEQ ID No. 984;
                                                                              SEQ ID No. 988;
    SEQ ID No. 989;
                       SEQ ID No. 990;
                                         SEQ ID No. 991;
                                                           SEQ ID No. 995;
                                                                              SEQ ID No. 996;
10 SEQ ID No. 999;
                                        SEQ ID No. 1003;
                     SEQ ID No. 1001;
                                                          SEQ ID No. 1004;
                                                                             SEQ ID No. 1005;
    SEQ ID No. 1006;
                      SEQ ID No. 1007;
                                        SEQ ID No. 1009;
                                                          SEQ ID No. 1010;
                                                                             SEQ ID No. 1011;
    SEQ ID No. 1012;
                      SEQ ID No. 1013;
                                        SEQ ID No. 1014;
                                                          SEQ ID No. 1016;
                                                                             SEQ ID No. 1017;
    SEQ ID No. 1018;
                      SEQ ID No. 1020;
                                        SEQ ID No. 1021;
                                                          SEQ ID No. 1025;
                                                                             SEQ ID No. 1026;
    SEQ ID No. 1027;
                      SEQ ID No. 1029;
                                        SEQ ID No. 1030;
                                                          SEQ ID No. 1031;
                                                                             SEQ ID No. 1035;
15 SEQ ID No. 1036;
                      SEQ ID No. 1037;
                                        SEQ ID No. 1038;
                                                          SEQ ID No. 1039;
                                                                             SEQ ID No. 1040;
                      SEQ ID No. 1045;
    SEQ ID No. 1044;
                                        SEQ ID No. 1047;
                                                          SEQ ID No. 1048;
                                                                             SEQ ID No. 1050;
    SEQ ID No. 1051; SEQ ID No. 1052;
                                        SEQ ID No. 1053;
                                                          SEQ ID No. 1055;
                                                                            SEQ ID No. 1056;
    SEQ ID No. 1057;
                      SEQ ID No. 1058;
                                        SEQ ID No. 1061;
                                                          SEQ ID No. 1062;
                                                                            SEQ ID No. 1063;
    SEQ ID No. 1064; SEQ ID No. 1065; SEQ ID No. 1066; SEQ ID No. 1068; SEQ ID No. 1069;
    SEQ ID No. 1072; SEQ ID No. 1074; SEQ ID No. 1076 and one of their representative fragments.
```

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* transmembrane polypeptide or one of its representative fragments, having between 4 and 6 transmembrane domains, and in that it is chosen from the polypeptides having the following sequences:

25 SEQ ID No. 7; SEQ ID No. 14; SEQ ID No. 16; SEQ ID No. 32; SEQ ID No. 34; SEQ ID No. 36; SEQ ID No. 38; SEQ ID No. 50; SEQ ID No. 57; SEQ ID No. 59; SEQ ID No. 61; SEQ ID No. 62; SEQ ID No. 63; SEQ ID No. 64; SEQ ID No. 67; SEQ ID No. 69; SEQ ID No. 72; SEQ ID No. 77; SEQ ID No. 80; SEQ ID No. 84; SEQ ID No. 87; SEQ ID No. 93; SEQ ID No. 95; SEQ ID No. 99; SEQ ID No. 108; SEQ ID No. 119; SEQ ID No. 125; SEQ ID No. 126; SEQ ID No. 129; 30 SEQ ID No. 131; SEQ ID No. 136; SEQ ID No. 146; SEQ ID No. 139; SEQ ID No. 152; SEQ ID No. 154; SEQ ID No. 160; SEQ ID No. 161; SEQ ID No. 172; SEQ ID No. 179; SEQ ID No. 182; SEQ ID No. 185; SEQ ID No. 200; SEQ ID No. 203; SEQ ID No. 205; SEQ ID No. 239; SEQ ID No. 242; SEQ ID No. 250; SEQ ID No. 253; SEQ ID No. 256; SEQ ID No. 259; SEQ ID No. 262; SEQ ID No. 268; SEQ ID No. 275; SEQ ID No. 281; SEQ ID No. 286; 35 SEQ ID No. 288; SEQ ID No. 292; SEQ ID No. 295; SEQ ID No. 296;

	SEQ ID No. 297;	SEQ ID No. 299;	SEQ ID No. 300;	SEQ ID No. 308;	SEQ ID No. 314;
	SEQ ID No. 317;	SEQ ID No. 318;	SEQ ID No. 324;	SEQ ID No. 342;	SEQ ID No. 343;
	SEQ ID No. 355;	SEQ ID No. 360;	SEQ ID No. 374;	SEQ ID No. 376;	SEQ ID No. 386;
	SEQ ID No. 388;	SEQ ID No. 392;	SEQ ID No. 394;	SEQ ID No. 395;	SEQ ID No. 402;
5	SEQ ID No. 405;	SEQ ID No. 411;	SEQ ID No. 415;	SEQ ID No. 416;	SEQ ID No. 422;
	SEQ ID No. 423;	SEQ ID No. 429;	SEQ ID No. 432;	SEQ ID No. 441;	SEQ ID No. 442;
	SEQ ID No. 444;	SEQ ID No. 449;	SEQ ID No. 452;	SEQ ID No. 456;	SEQ ID No. 460;
	SEQ ID No. 461;	SEQ ID No. 465;	SEQ ID No. 471;	SEQ ID No. 472;	SEQ ID No. 482;
	SEQ ID No. 489;	SEQ ID No. 492;	SEQ ID No. 494;	SEQ ID No. 495;	SEQ ID No. 502;
10	SEQ ID No. 505;	SEQ ID No. 506;	SEQ ID No. 509;	SEQ ID No. 516;	SEQ ID No. 517;
	SEQ ID No. 520;	SEQ ID No. 525;	SEQ ID No. 533;	SEQ ID No. 539;	SEQ ID No. 549;
	SEQ ID No. 554;	SEQ ID No. 557;	SEQ ID No. 563;	SEQ ID No. 570;	SEQ ID No. 573;
•	SEQ ID No. 581;	SEQ ID No. 590;	SEQ ID No. 591;	SEQ ID No. 600;	SEQ ID No. 607;
	SEQ ID No. 612;	SEQ ID No. 613;	SEQ ID No. 620;	SEQ ID No. 626;	SEQ ID No. 629;
15	SEQ ID No. 630;	SEQ ID No. 639;	SEQ ID No. 644;	SEQ ID No. 647;	SEQ ID No. 656;
	SEQ ID No. 659;	SEQ ID No. 661;	SEQ ID No. 685;	SEQ ID No. 687;	SEQ ID No. 699;
	SEQ ID No. 700;	SEQ ID No. 708;	SEQ ID No. 716;	SEQ ID No. 719;	SEQ ID No. 725;
	SEQ ID No. 747;	SEQ ID No. 749;	SEQ ID No. 756;	SEQ ID No. 765;	SEQ ID No. 767;
	SEQ ID No. 794;	SEQ ID No. 796;	SEQ ID No. 797;	SEQ ID No. 799;	SEQ ID No. 801;
20	SEQ ID No. 807;	SEQ ID No. 821;	SEQ ID No. 823;	SEQ ID No. 826;	SEQ ID No. 847;
	SEQ ID No. 853;	SEQ ID No. 861;	SEQ ID No. 870;	SEQ ID No. 871;	SEQ ID No. 875;
	SEQ ID No. 882;	SEQ ID No. 888;	SEQ ID No. 889;	SEQ ID No. 898;	SEQ ID No. 902;
	SEQ ID No. 903;	SEQ ID No. 911;	SEQ ID No. 916;	SEQ ID No. 931;	SEQ ID No. 939;
	SEQ ID No. 975;	SEQ ID No. 976;	SEQ ID No. 978;	SEQ ID No. 983;	SEQ ID No. 986;
25	SEQ ID No. 987;	SEQ ID No. 992;	SEQ ID No. 993;	SEQ ID No. 1000;	SEQ ID No. 1002;
	SEQ ID No. 1008;	SEQ ID No. 1019;	SEQ ID No. 1022;	SEQ ID No. 1032;	SEQ ID No. 1034;
	SEQ ID No. 1046	; SEQ ID No. 1054;	SEQ ID No. 1060;	SEQ ID No. 1071	and one of their
	representative frag	gments.			
	_		to a solotor to a s	olypantide according	g to the invention.

Preferably, the invention relates to a polypeptide according to the invention,

30 characterized in that it is a *Chlamydia trachomatis* transmembrane polypeptide or one of its representative fragments, having at least 7 transmembrane domains, and in that it is chosen from the polypeptides having the following sequences: SEQ ID No. 4; SEQ ID No. 6; SEQ ID No. 13; SEQ ID No. 20; SEQ ID No. 51; SEQ ID No. 71; SEQ ID No. 88; SEQ ID No. 118; SEQ ID No. 128; SEQ ID No. 132; SEQ ID No. 133; SEQ ID No. 158; SEQ ID No. 159; SEQ ID No. 174;

35 SEQ ID No. 180; SEQ ID No. 189; SEQ ID No. 210; SEQ ID No. 211; SEQ ID No. 214;

```
SEQ ID No. 215;
                       SEQ ID No. 226;
                                          SEQ ID No. 229;
                                                            SEQ ID No. 233;
                                                                                SEQ ID No. 235;
    SEQ ID No. 240;
                       SEQ ID No. 246;
                                          SEQ ID No. 251;
                                                            SEQ ID No. 255;
                                                                                SEQ ID No. 273;
    SEQ ID No. 354;
                       SEQ ID No. 364;
                                          SEQ ID No. 369;
                                                            SEQ ID No. 371;
                                                                                SEQ ID No. 397;
    SEQ ID No. 401;
                       SEQ ID No. 409;
                                          SEQ ID No. 412;
                                                            SEQ ID No. 419;
                                                                               SEQ ID No. 439;
5 SEQ ID No. 453;
                       SEQ ID No. 462;
                                          SEQ ID No. 490;
                                                            SEQ ID No. 510;
                                                                               SEQ ID No. 511;
    SEQ ID No. 518;
                       SEQ ID No. 535;
                                          SEQ ID No. 548;
                                                            SEQ ID No. 550;
                                                                               SEQ ID No. 564;
    SEQ ID No. 565;
                       SEQ ID No. 578;
                                         SEQ ID No. 579;
                                                            SEQ ID No. 614;
                                                                               SEQ ID No. 631;
    SEQ ID No. 636;
                       SEQ ID No. 650;
                                          SEQ ID No. 662;
                                                            SEQ ID No. 667;
                                                                               SEQ ID No. 679;
    SEQ ID No. 681;
                       SEQ ID No. 702;
                                         SEQ ID No. 727;
                                                            SEQ ID No. 741;
                                                                               SEQ ID No. 763;
10 SEQ ID No. 791;
                       SEQ ID No. 792;
                                         SEQ ID No. 815;
                                                            SEQ ID No. 816;
                                                                               SEQ ID No. 832;
    SEQ ID No. 846;
                       SEQ ID No. 858;
                                         SEQ ID No. 865;
                                                            SEQ ID No. 867;
                                                                               SEQ ID No. 868;
    SEQ ID No. 877;
                       SEQ ID No. 891;
                                         SEQ ID No. 896;
                                                            SEQ ID No. 907;
                                                                               SEQ ID No. 908;
    SEQ ID No. 918;
                       SEQ ID No. 919;
                                         SEQ ID No. 932;
                                                            SEQ ID No. 959;
                                                                               SEQ ID No. 977;
    SEQ ID No. 994;
                      SEQ ID No. 998; SEQ ID No. 1024;
                                                          SEQ ID No. 1028;
                                                                              SEQ ID No. 1042;
   SEQ ID No. 1067; SEQ ID No. 1070; SEQ ID No. 1073 and one of their representative fragments.
```

Preferably, the invention relates to a polypeptide according to the invention, in that it is a *Chlamydia trachomatis* surface exposed polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 2, SEQ ID No. 3, SEQ ID No. 21, SEQ ID No. 22, SEQ ID No. 23, SEQ ID No. 53, SEQ ID No. 77, SEQ ID No. 187, SEQ ID No. 203, SEQ ID No. 383, SEQ ID No. 477, SEQ ID No. 478, SEQ ID No. 479, SEQ ID No. 481, SEQ ID No. 482, SEQ ID No. 483, SEQ ID No. 484, SEQ ID No. 485, SEQ ID No. 486, SEQ ID No. 487, SEQ ID No. 488, SEQ ID No. 489, SEQ ID No. 490, SEQ ID No. 571, SEQ ID No. 572, SEQ ID No. 573, SEQ ID No. 593, SEQ ID No. 670, SEQ ID No. 693, SEQ ID No. 742, SEQ ID No. 749, SEQ ID No. 801, SEQ ID No. 817, SEQ ID No. 818, SEQ ID No. 819, SEQ ID No. 820, SEQ ID No. 851, SEQ ID No. 902, SEQ ID No. 923, SEQ ID No. 1035, SEQ ID No. 1036, SEQ ID No. 1037, SEQ ID No. 1038, SEQ ID No. 1069, SEQ ID No. 1070, SEQ ID No. 1071, SEQ ID No. 1073, SEQ ID No. 1076, SEQ ID No. 1095, SEQ ID No. 1096, SEQ ID No. 1141, SEQ ID No. 1181, and their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* lipoprotein or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 29, SEQ ID No. 42, SEQ ID No. 66, SEQ ID No. 72, SEQ ID No. 76, SEQ ID No. 78, SEQ ID No. 148, SEQ ID No. 154, SEQ ID No. 180, SEQ ID No. 182, SEQ ID No. 184, SEQ ID No. 187, SEQ ID No. 200, SEQ ID No. 242, SEQ ID No. 245, SEQ ID No. 250, SEQ ID No. 253, SEQ ID No. 272, SEQ ID No. 274, SEQ ID No. 275, SEQ ID No. 308, SEQ ID No. 350, SEQ ID No. 362,

SEO ID No. 383, SEO ID No. 394, SEQ ID No. 396, SEQ ID No. 399, SEQ ID No. 422, SEQ ID No. 488, SEQ ID No. 535, SEQ ID No. 568, SEQ ID No. 573, SEQ ID No. 578, SEQ ID No. 593, SEQ ID No. 607, SEQ ID No. 625, SEQ ID No. 662, SEQ ID No. 669, SEQ ID No. 688, SEQ ID No. 690, SEQ ID No. 716, SEQ ID No. 773, SEQ ID No. 778, SEQ ID No. 781, SEQ ID No. 783, SEQ ID No. 5 788, SEO ID No. 817, SEO ID No. 848, SEO ID No. 851, SEQ ID No. 853, SEQ ID No. 857, SEQ ID No. 875, SEQ ID No. 877, SEQ ID No. 886, SEQ ID No. 898, SEQ ID No. 902, SEQ ID No. 923, SEQ ID No. 938, SEQ ID No. 976, SEQ ID No. 978, SEQ ID No. 990, SEQ ID No. 1005, SEQ ID No. 1021, SEQ ID No. 1035, SEQ ID No. 1069, SEQ ID No. 1083, SEQ ID No. 1088, SEQ ID No. 1089, SEO ID No. 1091, SEO ID No. 1092, SEQ ID No. 1095, SEQ ID No. 1096, SEQ ID No. 1100, SEQ 10 ID No. 1105, SEQ ID No. 1108, SEQ ID No. 1117, SEQ ID No. 1120, SEQ ID No. 1121, SEQ ID No. 1124, SEQ ID No. 1128, SEQ ID No. 1133, SEQ ID No. 1135, SEQ ID No. 1139, SEQ ID No. 1140, SEQ ID No. 1157, SEQ ID No. 1159, SEQ ID No. 1163, SEQ ID No. 1165, SEQ ID No. 1167, SEQ ID No. 1168, SEQ ID No. 1169, SEQ ID No. 1171, SEQ ID No. 1173, SEQ ID No. 1174, SEQ ID No. 1177, SEO ID No. 1180, SEQ ID No. 1181, SEQ ID No. 1186, SEQ ID No. 1194, SEQ ID No. 1197, and their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, in that it is a Chlamydia trachomatis polypeptide involved in lipopolysaccharide (LPS) biosynthesis, and in that it is chosen from the polypeptides having the following sequences: SEQ ID No. 17, SEQ ID No. 201, SEQ ID No. 691, SEQ ID No. 807, SEQ ID No. 936, SEQ ID No. 983, SEQ ID No. 1019, SEQ ID No. 1077, and their representative fragments.

Preferably, the invention relates to additional LPS-related polypeptides according to the invention, in that it is:

- a Chlamydia trachomatis KDO (3-deoxy-D-manno-octylosonic acid)-related (a) polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences: SEQ ID No. 41, SEQ ID No. 242, SEQ ID No. 269, SEQ ID No. 772, and one of their representative fragments;
 - a Chlamydia trachomatis phosphomannomutase-related polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequence: SEO ID No. 139, and its representative fragments;
- a Chlamydia trachomatis phosphoglucomutase-related polypeptide or one of 30 (c) its representative fragments, and in that it is chosen from the polypeptides having the following sequence: SEQ ID No. 567 and its representative fragments; and
- a Chlamydia trachomatis lipid A component-related polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following 35 sequences: SEQ ID No. 4, SEQ ID No. 933, SEQ ID No. 934, SEQ ID No. 935, SEQ ID No. 1185,

and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments that contains an RGD sequence and is also an outer membrane protein, and in that it is chosen from the polypeptides having the following sequences: SEQ. ID No. 488, SEQ ID No. 489, SEQ ID No. 571, SEQ ID No. 572, SEQ No. 573, SEQ ID No. 716 and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, in that it is a Chlamydia trachomatis polypeptide or one of its representative fragments that is cysteine-rich and contains RGD sequence, and in that it is chosen from the polypeptides having the following sequence: SEQ ID No. 144 and one of its representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, in that it is a *Chlamydia trachomatis* outer membrane polypeptide that contains cysteines in their first 30 amino acids and also contain an RGD sequence, and in that it is chosen from the polypeptides having the following sequences: SEQ ID No. 101, SEQ ID No. 122, SEQ ID No. 308, SEQ ID No. 488, SEQ ID No. 489, SEQ ID No. 571, SEQ ID No. 572, SEQ ID No. 573, SEQ ID No. 651, SEQ ID No. 679, SEQ ID No. 680, SEQ ID No. 705, SEQ ID No. 716, SEQ ID No. 763, SEQ ID No. 870, SEQ ID No. 878, SEQ ID No. 879, SEQ ID No. 995, SEQ ID No. 1028, SEQ ID No. 1029, SEQ ID No. 1176, and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments that contains RGD sequences homologous to *Chlamydia pneumoniae* polypeptides containing RGD sequences, and in that it is chosen from the polypeptides having the following sequences: SEQ ID No. 28, SEQ ID No. 101, SEQ ID No. 125, SEQ ID No. 155, SEQ ID No. 156, SEQ ID No. 286, SEQ ID No. 571, SEQ ID No. 572, SEQ ID No. 573, SEQ ID No. 763, SEQ ID No. 870, and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, in that it is a *Chlamydia trachomatis* Type III or non-Type III secreted polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 180, SEQ ID No. 181, SEQ ID No. 207, SEQ ID No. 208, SEQ ID No. 372, SEQ ID No. 391, SEQ ID No. 399, SEQ ID No. 477, SEQ ID No. 486, SEQ ID No. 749, SEQ ID No. 758, SEQ ID No. 819, SEQ ID No. 878, SEQ ID No. 888, SEQ ID No. 896, SEQ ID No. 897, SEQ ID No. 900, SEQ ID No. 902, SEQ ID No. 923, SEQ ID No. 1015, SEQ ID No. 1018, SEQ ID No. 1059, SEQ ID No. 1060, SEQ ID No. 1069, SEQ ID No. 1071, SEQ ID No. 1073, SEQ ID No. 1076, SEQ ID No. 1189, and their representative fragments.

10

is a *Chlamydia trachomatis* cell wall anchored surface polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences: SEQ ID No. 662, SEQ ID No. 681, SEQ ID No. 1182, SEQ ID No. 1192, and their representative

42

fragments.

Preferably, the invention relates to a polypeptide according to the invention, in that it 5 is a Chlamydia trachomatis polypeptide or one of its representative fragments not found in Chlamydia pneumoniae (Blastp P>e⁻¹⁰) and in that it is chosen from the polypeptides having the following sequences: SEQ ID No.2, SEQ ID No. 18, SEQ ID No. 60, SEQ ID No. 66, SEQ ID No. 67, SEQ ID No.68, SEQ ID No. 69, SEQ ID No. 70, SEQ ID No. 81, SEQ ID No. 89, SEQ ID No. 107, SEQ ID No.108, SEQ ID No. 109, SEQ ID No.134, SEQ ID No. 147, SEQ ID No.191, SEQ ID No. 194, SEQ ID No. 216, SEQ ID No. 217, SEQ ID No. 218, SEQ ID No. 219, SEQ ID No. 220, SEQ ID No. 221, SEQ ID No. 222, SEQ ID No. 222, SEQ ID No. 223, SEQ ID No. 224, SEQ ID No. 225, SEQ ID No. 228, SEQ ID No. 235, SEQ ID No. 257, SEQ ID No. 276, SEQ ID No. 277, SEQ ID No. 278, SEQ ID No. 279, SEQ ID No. 280, SEQ ID No. 281, SEQ ID No. 282, SEQ ID No.283, SEQ ID No. 284, SEQ ID No. 285, SEQ ID No. 289, SEQ ID No.291, SEQ ID No. 298, SEQ ID No. 284, SEQ ID No. 313, SEQ ID No. 314, SEQ ID No. 315, SEQ ID No. 316, SEQ ID No. 334, SEQ ID No. 335, SEQ ID No. 336, SEQ ID No. 337, SEQ ID No. 338, SEQ ID No. 339, SEQ ID No. 340, SEQ ID No. 381, SEQ ID No. 393, SEQ ID No. 413, SEQ ID No. 418, SEQ ID No. 419, SEQ ID No. 419, SEQ ID No. 420, SEQ ID No. 421, SEQ ID No. 422, SEQ ID No. 423, SEQ ID No. 436, SEQ ID No. 460, SEQ ID 20 No. 475, SEQ ID No. 476, SEQ ID No. 480, SEQ ID No. 485, SEQ ID No. 487, SEQ ID No.491, SEQ ID No. 492, SEQ ID No. 493, SEQ ID No. 494, SEQ ID No. 496, SEQ ID No. 500, SEQ ID No. 504, SEQ ID No. 514, SEQ ID No. 527, SEQ ID No. 559, SEQ ID No.569, SEQ ID No. 570, SEQ ID No. 575, SEQ ID No. 580, SEQ ID No. 582, SEQ ID No. 593, SEQ ID No. 598, SEQ ID No.632, SEQ ID No.640, SEQ ID No.651, SEQ ID No.671, SEQ ID No. 690, SEQ ID No. 694, ID No. 698, SEQ ID 25 No. 710, SEQ ID No. 722, SEQ ID No. 723, SEQ ID No. 724, SEQ ID No. 770, SEQ ID No. 771, SEQ ID No.782, SEQ ID No. 783, SEQ ID No. 784, SEQ ID No. 790, SEQ ID No. 795, SEQ ID No. 798, SEQ ID No. 805, SEQ ID No. 810, SEQ ID No. 817, SEQ ID No. 829, SEQ ID No. 830, SEQ ID No. 864, SEQ ID No. 866, SEQ ID No. 876, SEQ ID No. 887, SEQ ID No. 892, SEQ ID No. 899, SEQ ID No. 913, SEQ ID No. 921, SEQ ID No. 933, SEQ ID No. 938, SEQ ID No. 949, SEQ ID No. 956, SEQ ID No. 1010, SEQ ID No. 1017, SEQ ID No. 1018, SEQ ID No. 1027, SEQ ID No. 1030, SEQ ID No. 1037, SEQ ID No. 1038, SEQ ID No. 1047, SEQ ID No. 1072, SEQ ID No. 1074, SEQ ID No. 1075, SEQ ID No. 1078, SEQ ID No. 1079, SEQ ID No. 1081, SEQ ID No. 1083, SEQ ID No. 1084, SEQ ID No. 1087, SEQ ID No. 1088, SEQ ID No. 1089, SEQ ID No. 1091, SEQ ID No. 1092, SEQ ID No. 1094, SEQ ID No. 1095, SEQ ID No. 1096, SEQ ID No. 1098, SEQ ID No. 1104, SEQ ID No. 1105, SEQ ID No. 1106, SEQ ID No. 1108, SEQ ID No. 1110, SEQ ID No. 1114, SEQ ID No. 1115, SEQ ID No. 1116, SEQ ID No. 1117, SEQ ID No. 1119, SEQ ID No. 1128, SEQ ID No. 1132, SEQ ID No. 1133, SEQ ID No. 1135, SEQ ID No. 1136, SEQ ID No. 1139, SEQ ID No. 1140, SEQ ID No. 1141, SEQ ID No. 1142, SEQ ID No. 1144, SEQ ID No. 1148, SEQ ID No. 1151, SEQ ID No. 1155, SEQ ID No. 1157, SEQ ID No. 1159, SEQ ID No. 1161, SEQ ID No. 1162, SEQ ID No. 1165, SEQ ID No. 1166, SEQ ID No. 1167, SEQ ID No. 1168, SEQ ID No. 1169, SEQ ID No. 1171, SEQ ID No. 1172, SEQ ID No. 1173, SEQ ID No. 1174, SEQ ID No. 1175, SEQ ID No. 1176, SEQ ID No. 1177, SEQ ID No. 1178, SEQ ID No. 1180, SEQ ID No. 1181, SEQ ID No. 1183, SEQ ID No. 1184, SEQ ID No. 1186, SEQ ID No. 1187, SEQ ID No. 1188, SEQ ID No. 1192, SEQ ID No. 1194, SEQ ID No. 1197, and their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the intermediate metabolism, in particular in the metabolism of sugars and/or of cofactors, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 10; SEQ ID No. 44; SEQ ID No. 45; SEQ ID No. 46; SEQ ID No. 47; SEQ ID No. 93; 15 SEQ ID No. 101; SEQ ID No. 102; SEQ ID No. 103; SEQ ID No. 106; SEQ ID No. 107; SEQ ID No. 120; SEQ ID No. 121; SEQ ID No. 130; SEQ ID No. 135; SEQ ID No. 140; SEQ ID No. 143; SEQ ID No. 144; SEQ ID No. 145; SEQ ID No. 158; SEQ ID No. 159; SEQ ID No. 160; SEQ ID No. 161; SEQ ID No. 192; SEQ ID No. 193; SEQ ID No. 196; SEQ ID No. 197; SEQ ID No. 198; SEQ ID No. 199; SEQ ID No. 227; SEQ ID No. 229; 20 SEQ ID No. 236; SEQ ID No. 236; SEQ ID No. 239; SEQ ID No. 243; SEQ ID No. 245; SEQ ID No. 264; SEQ ID No. 265; SEQ ID No. 297; SEQ ID No. 331; SEQ ID No. 333; SEQ ID No. 359; SEQ ID No. 360; SEQ ID No. 374; SEQ ID No. 404; SEQ ID No. 405; SEQ ID No. 405; SEQ ID No. 410; SEQ ID No. 415; SEQ ID No. 415; SEQ ID No. 416; SEQ ID No. 417; SEQ ID No. 432; SEQ ID No. 460; SEQ ID No. 461; SEQ ID No. 462; 25 SEQ ID No. 495; SEQ ID No. 513; SEQ ID No. 515; SEQ ID No. 566; SEQ ID No. 566; SEQ ID No. 566; SEQ ID No. 589; SEQ ID No. 613; SEQ ID No. 645; SEQ ID No. 646; SEQ ID No. 647; SEQ ID No. 652; SEQ ID No. 653; SEQ ID No. 654; SEQ ID No. 672; SEQ ID No. 673; SEQ ID No. 682; SEQ ID No. 674; SEQ ID No. 684; SEQ ID No. 692; SEQ ID No. 700; SEQ ID No. 725; SEQ ID No. 801; SEQ ID No. 802; SEQ ID No. 835; SEQ ID No. 836; SEQ ID No. 837; SEQ ID No. 860; SEQ ID No. 861; SEQ ID No. 862; SEQ ID No. 863; SEQ ID No. 869; SEQ ID No. 869; SEQ ID No. 925; SEQ ID No. 964; SEQ ID No. 983 and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the intermediate metabolism of nucleotides or nucleic acids, and in that it is

35

chosen from the polypeptides having the following sequences:

```
SEQ ID No. 142;
                                         SEQ ID No. 169;
                                                            SEQ ID No. 256;
                                                                               SEQ ID No. 268;
   SEQ ID No. 142;
                                                                               SEQ ID No. 444;
                      SEQ ID No. 352;
                                         SEQ ID No. 366;
                                                            SEQ ID No. 435;
   SEQ ID No. 325;
                                                                               SEQ ID No. 549;
                                                            SEQ ID No. 548;
                                         SEQ ID No. 530;
   SEQ ID No. 528;
                      SEQ ID No. 529;
                                                            SEQ ID No. 619;
                                         SEQ ID No. 617;
                                                                               SEQ ID No. 644;
                      SEQ ID No. 602;
5 SEQ ID No. 601;
   SEQ ID No. 745; SEQ ID No. 971; SEQ ID No. 972; SEQ ID No. 1023 and one of their representative
   fragments.
```

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of nucleic acids, and in that it is chosen from the polypeptides having the following sequences:

```
SEQ ID No. 5; SEQ ID No. 12; SEQ ID No. 82; SEQ ID No. 96; SEQ ID No. 97; SEQ ID No. 98;
                                                            SEQ ID No. 118;
                                                                               SEQ ID No. 136;
                      SEQ ID No. 100;
                                         SEQ ID No. 105;
    SEQ ID No. 99;
                                                            SEQ ID No. 204;
                                                                               SEQ ID No. 259;
                                         SEQ ID No. 190;
    SEQ ID No. 137;
                       SEQ ID No. 163;
                                                            SEQ ID No. 300;
                                                                               SEQ ID No. 301;
                                         SEQ ID No. 290;
                       SEQ ID No. 262;
    SEQ ID No. 260;
                       SEQ ID No. 387;
                                         SEQ ID No. 427;
                                                            SEQ ID No. 434;
                                                                               SEQ ID No. 441;
    SEQ ID No. 302;
                                                            SEQ ID No. 596;
                                                                               SEQ ID No. 597;
    SEQ ID No. 444;
                                         SEQ ID No. 595;
                       SEQ ID No. 471;
                                                            SEQ ID No. 612;
                                                                               SEQ ID No. 624;
                                         SEQ ID No. 605;
                       SEQ ID No. 600;
    SEO ID No. 599;
                                                                               SEQ ID No. 702;
                       SEQ ID No. 650;
                                         SEO ID No. 657;
                                                            SEQ ID No. 658;
    SEQ ID No. 625;
                                                                               SEQ ID No. 766;
                                                            SEQ ID No. 719;
                                          SEQ ID No. 708;
20 SEQ ID No. 703;
                       SEQ ID No. 704;
                                          SEQ ID No. 779;
                                                                               SEQ ID No. 788;
                                                            SEQ ID No. 787;
                       SEQ ID No. 775;
    SEQ ID No. 767;
                       SEQ ID No. 841;
                                          SEQ ID No. 842;
                                                            SEQ ID No. 883;
                                                                               SEQ ID No. 884;
    SEQ ID No. 794;
                                                                               SEQ ID No. 929;
                                                            SEQ ID No. 928;
                                          SEQ ID No. 924;
    SEQ ID No. 907;
                       SEQ ID No. 918;
                                                                               SEQ ID No. 970;
                                          SEQ ID No. 963;
                                                            SEQ ID No. 969;
                       SEQ ID No. 962;
    SEQ ID No. 962;
    SEQ ID No. 975; SEQ ID No. 979; SEQ ID No. 995; SEQ ID No. 1031; SEQ ID No. 1032 and one of
25
     their representative fragments.
```

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of amino acids or polypeptides, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 27; SEQ ID No. 41; SEQ ID No. 55; SEQ ID No. 56; SEQ ID No. 57; SEQ ID No. 59; SEQ ID No. 62; SEQ ID No. 63; SEQ ID No. 64; SEQ ID No. 65; SEQ ID No. 119; SEQ ID No. 132; SEQ ID No. 278; SEQ ID No. 279; SEQ ID No. 241; SEQ ID No. 277; SEO ID No. 240; SEQ ID No. 446; SEQ ID No. 428; SEQ ID No. 442; SEQ ID No. 406; SEQ ID No. 382; SEQ ID No. 542; SEQ ID No. 454; SEQ ID No. 541; SEQ ID No. 447; SEQ ID No. 453;

```
SEQ ID No. 591;
                   SEQ ID No. 608;
                                      SEQ ID No. 609;
                                                         SEQ ID No. 610;
                                                                            SEQ ID No. 618;
SEQ ID No. 648;
                   SEQ ID No. 649;
                                      SEQ ID No. 660;
                                                         SEQ ID No. 661;
                                                                            SEQ ID No. 677;
SEQ ID No. 717;
                   SEQ ID No. 765;
                                      SEQ ID No. 797;
                                                         SEQ ID No. 871;
                                                                            SEQ1D No. 875;
SEQ ID No. 920;
                   SEQ ID No. 922;
                                      SEQ ID No. 937;
                                                        SEQ ID No. 998;
                                                                           SEQ ID No. 1020;
SEQ ID No. 1021; SEQ ID No. 1034; SEQ ID No. 1044; SEQ ID No. 1046; SEQ ID No. 1049 and
one of their representative fragments.
```

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of polypeptides, and in that it is chosen from the polypeptides having the following sequences:

```
SEQ ID No. 21; SEQ ID No. 22; SEQ ID No. 23; SEQ ID No. 24; SEQ ID No. 25; SEQ ID No. 26;
    SEQ ID No. 75; SEQ ID No. 84; SEQ ID No. 86; SEQ ID No. 92; SEQ ID No. 133; SEQ ID No. 151;
    SEQ ID No. 152;
                       SEQ ID No. 157;
                                         SEQ ID No. 179;
                                                                              SEQ ID No. 307;
                                                            SEQ ID No. 209;
    SEQ ID No. 326;
                       SEQ ID No. 343;
                                         SEQ ID No. 344;
                                                            SEQ ID No. 345;
                                                                              SEQ ID No. 371;
15 SEQ ID No. 429;
                      SEQ ID No. 519;
                                         SEQ ID No. 557;
                                                            SEQ ID No. 586;
                                                                              SEQ ID No. 587;
    SEQ ID No. 630;
                      SEQ ID No. 656;
                                         SEQ ID No. 706;
                                                            SEQ ID No. 707;
                                                                              SEQ ID No. 730;
    SEQ ID No. 751;
                      SEQ ID No. 752;
                                         SEQ ID No. 786;
                                                            SEQ ID No. 847;
                                                                              SEQ ID No. 885;
    SEQ ID No. 923; SEQ ID No. 978; SEQ ID No. 1039; SEQ ID No. 1048 and one of their
    representative fragments.
```

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the metabolism of fatty acids, and in that it is chosen from the polypeptides having the following sequences:

```
SEQ ID No. 4; SEQ ID No. 15; SEQ ID No. 16; SEQ ID No. 141; SEQ ID No. 173; SEQ ID No. 205;
25 SEQ ID No. 205;
                        SEQ ID No. 206;
                                          SEQ ID No. 207;
                                                             SEQ ID No. 208;
                                                                                 SEQ ID No. 312;
    SEQ ID No. 355;
                       SEQ ID No. 415;
                                          SEQ ID No. 550;
                                                             SEQ ID No. 558;
                                                                                 SEQ ID No. 560;
    SEQ ID No. 561;
                       SEQ ID No. 574;
                                          SEQ ID No. 574;
                                                             SEQ ID No. 577;
                                                                                SEQ ID No. 578;
    SEQ ID No. 590;
                       SEQ ID No. 614;
                                          SEQ ID No. 772;
                                                             SEQ ID No. 808;
                                                                                 SEQ ID No. 809:
    SEQ ID No. 904;
                       SEQ ID No. 905;
                                          SEQ ID No. 905;
                                                             SEQ ID No. 933;
                                                                                 SEQ ID No. 934;
    SEQ ID No. 934; SEQ ID No. 936 and one of their representative fragments.
30
```

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the synthesis of the wall, and in that it is chosen from the polypeptides having the following sequences:

35 SEQ ID No. 87; SEQ ID No. 196; SEQ ID No. 242; SEQ ID No. 269; SEQ ID No. 628;

SEQ ID No. 629; SEQ ID No. 634; SEQ ID No. 635; SEQ ID No. 637; SEQ ID No. 638; SEQ ID No. 1019 and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* polypeptide or one of its representative fragments which is involved in the transcription, translation and/or maturation process, and in that it is chosen from the polypeptides having the following sequences:

```
SEQ ID No. 332;
                                                             SEQ ID No. 212;
                                                                               SEQ ID No. 213;
    SEQ ID No. 112;
                       SEQ ID No. 113;
                                          SEQ ID No. 363;
                                                             SEQ ID No. 364;
                                                                               SEQ ID No. 407;
                       SEQ ID No. 362;
    SEO ID No. 350;
                       SEQ ID No. 546;
                                          SEQ ID No. 643;
                                                             SEQ ID No. 744;
                                                                                SEQ ID No. 746;
    SEQ ID No. 451;
10 SEQ ID No. 833;
                       SEQ ID No. 868;
                                         SEQ ID No. 981;
                                                            SEQ ID No. 982;
                                                                              SEQ ID No. 1003;
    SEQ ID No. 1011; SEQ ID No. 1042 and one of their representative fragments.
```

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* ribosomal polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences:

```
SEQ ID No. 116;
                                                       SEQ ID No. 328;
                                                                          SEQ ID No. 361;
SEQ ID No. 114;
                   SEQ ID No. 115;
                   SEQ ID No. 445;
SEQ ID No. 375;
                                     SEQ ID No. 543;
                                                        SEQ ID No. 584;
                                                                          SEQ ID No. 585;
                                                        SEQ ID No. 942;
                                                                          SEQ ID No. 944;
                                     SEQ ID No. 941;
SEQ ID No. 743;
                   SEQ ID No. 813;
                                     SEQ ID No. 948;
                                                        SEQ ID No. 950;
                                                                          SEQ ID No. 951;
                   SEQ ID No. 947;
SEO ID No. 946;
                   SEQ ID No. 953;
                                     SEQ ID No. 954;
                                                        SEQ ID No. 955;
                                                                          SEQ ID No. 955;
SEQ ID No. 952;
                                                                         SEQ ID No. 1040;
                                     SEQ ID No. 960;
                                                       SEQ ID No. 961;
SEQ ID No. 957;
                   SEQ ID No. 958;
SEQ ID No. 1041; SEQ ID No. 1043; SEQ ID No. 1063; SEQ ID No. 1064 and one of their
fragments.
```

Preferably, the invention also relates to a polypeptide according to the invention, characterized in that it is a *Chlamydia trachomatis* transport polypeptide or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences:

```
SEQ ID No. 6; SEQ ID No. 50; SEQ ID No. 51; SEQ ID No. 80; SEQ ID No. 125; SEQ ID No. 126;
                                          SEQ ID No. 215;
                                                            SEQ ID No. 246;
                                                                               SEQ ID No. 248;
    SEQ ID No. 128;
                       SEQ ID No. 129;
                                          SEQ ID No. 252;
                                                            SEQ ID No. 253;
                                                                               SEQ ID No. 255;
    SEQ ID No. 249;
                       SEQ ID No. 251;
                                          SEQ ID No. 293;
                                                            SEQ ID No. 309;
                                                                               SEQ ID No. 323;
    SEQ ID No. 271;
                       SEQ ID No. 275;
                       SEQ ID No. 398;
                                          SEQ ID No. 401;
                                                            SEQ ID No. 449;
                                                                               SEQ ID No. 511;
30 SEQ ID No. 324;
                                                                               SEQ ID No. 679;
                       SEO ID No. 564;
                                          SEQ ID No. 565;
                                                            SEQ ID No. 667;
    SEQ ID No. 512;
                                                                               SEQ ID No. 714;
    SEQ ID No. 680;
                       SEQ ID No. 711;
                                          SEQ ID No. 712;
                                                            SEQ ID No. 713;
                                          SEQ ID No. 731;
                                                                               SEQ ID No. 737;
                       SEQ ID No. 730;
                                                            SEQ ID No. 736;
    SEQ ID No. 715;
                       SEQ ID No. 870;
                                          SEQ ID No. 908;
                                                            SEQ ID No. 919;
                                                                               SEQ ID No. 977;
    SEQ ID No. 738;
                       SEQ ID No. 988;
                                          SEO ID No. 992;
                                                            SEO ID No. 993;
                                                                               SEQ ID No. 994;
    SEQ ID No. 987;
```

SEQ ID No. 1028; SEQ ID No. 1029 and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a Chlamydia trachomatis polypeptide or one of its representative fragments which is involved in the virulence process, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 20; SEQ ID No. 815; SEQ ID No. 816; SEQ ID No. 898; SEQ ID No. 1059; SEQ ID No. 1060 and one of their representative fragments.

Preferably, the invention relates to a polypeptide according to the invention, characterized in that it is a Chlamydia trachomatis polypeptide or one of its representative fragments which is involved in the secretory system and/or which is secreted, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 758; SEQ ID No. 888; SEQ ID No. 889; SEQ ID No. 890; SEQ ID No. 891; SEQ ID No. 896; SEQ ID No. 897; SEQ ID No. 898 and one of their representative fragments.

The secreted polypeptides, including the Type III and other, non-Type III secreted polypeptides, of the present invention, as well as the corresponding nucleotide sequences, may be detected by techniques known to persons skilled in the art, such as for example the techniques using cloning combined with vectors allowing the expression of the said polypeptides fused to export markers such as the luc gene for luciferase or the PhoA gene for alkaline phosphatase.

Preferably, the invention relates to a polypeptide according to the invention, 20 characterized in that it is a polypeptide specific to Chlamydiae or one of its representative fragments, and in that it is chosen from the polypeptides having the following sequences:

SEQ ID No. 22; SEQ ID No. 29; SEQ ID No. 31; SEQ ID No. 32; SEQ ID No. 34; SEQ ID No. 35; SEQ ID No. 39; SEQ ID No. 40; SEQ ID No. 43; SEQ ID No. 48; SEQ ID No. 49; SEQ ID No. 50; SEQ ID No. 52; SEQ ID No. 53; SEQ ID No. 54; SEQ ID No. 72; SEQ ID No. 77; SEQ ID No. 78; 25 SEQ ID No. 87; SEQ ID No. 90; SEQ ID No. 95; SEQ ID No. 108; SEQ ID No. 110; SEQ ID No. 111; SEQ ID No. 122; SEQ ID No. 123; SEQ ID No. 124; SEQ ID No. 127; SEQ ID No. 138; SEQ ID No. 144; SEQ ID No. 146; SEQ ID No. 153; SEQ ID No. 155; SEQ ID No. 164; SEQ ID No. 166; SEQ ID No. 175; SEQ ID No. 182; SEQ ID No. 184; SEQ ID No. 186; SEQ ID No. 187; SEQ ID No. 188; SEQ ID No. 202; SEQ ID No. 210; 30 SEO ID No. 247; SEQ ID No. 258; SEQ ID No. 266; SEQ ID No. 267; SEQ ID No. 270; SEQ ID No. 273; SEQ ID No. 274; SEQ ID No. 295; SEQ ID No. 296; SEQ ID No. 305; SEQ ID No. 306; SEQ ID No. 309; SEQ ID No. 318; SEQ ID No. 319; SEQ ID No. 322; SEQ ID No. 326; SEQ ID No. 342; SEQ ID No. 357; SEQ ID No. 376; SEQ ID No. 379; SEQ ID No. 380; SEQ ID No. 388; SEQ ID No. 390; SEQ ID No. 400; SEQ ID No. 431; 35 SEQ ID No. 433; SEQ ID No. 438; SEQ ID No. 443;

SEQ ID No. 456;

SEQ ID No. 457;

	SEQ ID No. 458;	SEQ ID No. 464;	SEQ ID No. 468;	SEQ ID No. 470;	SEQ ID No. 473;
	SEQ ID No. 486;	SEQ ID No. 489;	SEQ ID No. 497;	SEQ ID No. 501;	SEQ ID No. 503;
	SEQ ID No. 504;	SEQ ID No. 508;	SEQ ID No. 512;	SEQ ID No. 521;	SEQ'ID No. 522;
	SEQ ID No. 523;	SEQ ID No. 524;	SEQ ID No. 533;	SEQ ID No. 535;	SEQ ID No. 536;
5	SEQ ID No. 537;	SEQ ID No. 538;	SEQ ID No. 539;	SEQ ID No. 540;	SEQ ID No. 554;
	SEQ ID No. 563;	SEQ ID No. 572;	SEQ ID No. 579;	SEQ ID No. 595;	SEQ ID No. 603;
	SEQ ID No. 604;	SEQ ID No. 606;	SEQ ID No. 607;	SEQ ID No. 615;	SEQ ID No. 616;
	SEQ ID No. 622;	SEQ ID No. 641;	SEQ ID No. 642;	SEQ ID No. 659;	SEQ ID No. 668;
	SEQ ID No. 670;	SEQ ID No. 693;	SEQ ID No. 695;	SEQ ID No. 696;	SEQ ID No. 699;
10	SEQ ID No. 703;	SEQ ID No. 704;	SEQ ID No. 716;	SEQ ID No. 726;	SEQ ID No. 728;
	SEQ ID No. 739;	SEQ ID No. 742;	SEQ ID No. 747;	SEQ ID No. 750;	SEQ ID No. 751;
	SEQ ID No. 755;	SEQ ID No. 757;	SEQ ID No. 759;	SEQ ID No. 761;	SEQ ID No. 762;
	SEQ ID No. 763;	SEQ ID No. 764;	SEQ ID No. 773;	SEQ ID No. 780;	SEQ ID No. 781;
	SEQ ID No. 789;	SEQ ID No. 800;	SEQ ID No. 803;	SEQ ID No. 804;	SEQ ID No. 818;
15	SEQ ID No. 820;	SEQ ID No. 822;	SEQ ID No. 823;	SEQ ID No. 824;	SEQ ID No. 827;
	SEQ ID No. 828;	SEQ ID No. 839;	SEQ ID No. 849;	SEQ ID No. 850;	SEQ ID No. 851;
	SEQ ID No. 852;	SEQ ID No. 855;	SEQ ID No. 856;	SEQ ID No. 857;	SEQ ID No. 858;
	SEQ ID No. 859;	SEQ ID No. 860;	SEQ ID No. 861;	SEQ ID No. 862;	SEQ ID No. 863;
	SEQ ID No. 865;	SEQ ID No. 868;	SEQ ID No. 869;	SEQ ID No. 870;	SEQ ID No. 871;
20	SEQ ID No. 872;	SEQ ID No. 873;	SEQ ID No. 874;	SEQ ID No. 875;	SEQ ID No. 877;
	SEQ ID No. 878;	SEQ ID No. 880;	SEQ ID No. 882;	SEQ ID No. 884;	SEQ ID No. 886;
	SEQ ID No. 893;	SEQ ID No. 901;	SEQ ID No. 906;	SEQ ID No. 910;	SEQ ID No. 912;
	SEQ ID No. 915;	SEQ ID No. 916;	SEQ ID No. 917;	SEQ ID No. 926;	SEQ ID No. 929;
	SEQ ID No. 933;	SEQ ID No. 965;	SEQ ID No. 967;	SEQ ID No. 968;	SEQ ID No. 984;
25	SEQ ID No. 986;	SEQ ID No. 989;	SEQ ID No. 990;	SEQ ID No. 996;	SEQ ID No. 997;
	SEQ ID No. 1001;	SEQ ID No. 1002;	SEQ ID No. 1013;	SEQ ID No. 1016;	SEQ ID No. 1031;
	SEQ ID No. 1033;	SEQ ID No. 1035;	SEQ ID No. 1049;	SEQ ID No. 1051;	SEQ ID No. 1052;
	SEQ ID No. 1054;				SEQ ID No. 1062;
	SEQ ID No. 1070	; SEQ ID No. 1071; S	EQ ID No. 1073 and	one of their represent	ative fragments.
•	o In capacity in the present invention, the functional group to which a polypeptide of the				

In general, in the present invention, the functional group to which a polypeptide of the invention belongs, as well as its corresponding nucleotide sequence, may be determined either by comparative analogy with sequences already known, or by the use of standard techniques of biochemistry, of cytology combined with the techniques of genetic engineering such as immunoaffinity, localization by immunolabelling, differential extraction, measurement of enzymatic 35 activity, study of the activity inducing or repressing expression or the study of expression in E. coli.

30

35

It is clearly understood, on the one hand, that, in the present invention, the nucleotide sequences (ORF) and the amino acid sequences (SEQ ID No. 2 to SEQ ID No. 1197) which are listed by functional group, are not exhaustive within the group considered. Moreover, it is also clearly understood that, in the present invention, a nucleotide sequence (ORF) or an amino acid sequence mentioned within a given functional group may also be part of another group taking into account, for example, the interrelationship between the groups listed. Accordingly, and as an example of this interrelationship, an exported and/or secreted polypeptide as well as its coding nucleotide sequence may also be involved in the *Chlamydia trachomatis* virulence process by modifying the defense mechanism of the infected host cell, or a transmembrane polypeptide or its coding nucleotide sequence is also part of the polypeptides or coding nucleotide sequences of the cellular envelope.

The subject of the present invention is also the nucleotide and/or polypeptide sequences according to the invention, characterized in that the said sequences are recorded on a medium, called recording medium, whose type and nature facilitate the reading, the analysis and the exploitation of the said sequences. These media may of course also contain other information extracted from the present invention, such as in particular the analogies with already known sequences, such as those mentioned in Table 1 of the present description, and/or may contain, in addition, information relating to the nucleotide and/or polypeptide sequences of other microorganisms so as to facilitate the comparative analysis and the exploitation of the results obtained.

Among these recording media, computer-readable media, such as magnetic, optical, electrical and hybrid media such as, for example, floppy disks, CD-ROMs or recording cassettes, are preferred in particular.

The invention also relates to nucleotide sequences which can be used as primer or probe, characterized in that the said sequences are chosen from the nucleotide sequences according to the invention.

25 The invention relates, in addition, to the use of a nucleotide sequence according to the invention, as primer or probe, for the detection and/or amplification of nucleic acid sequences.

The nucleotide sequences according to the invention may thus be used to amplify nucleotide sequences, in particular by the PCR technique (polymerase chain reaction) (Erlich, 1989; Innis et al., 1990; Rolfs et al., 1991, and White et al., 1997).

These oligodeoxyribonucleotide or oligoribonucleotide primers correspond to representative nucleotide fragments, and are advantageously at least 8 nucleotides, preferably at least 12 nucleotides, 15 nucleotides and still more preferably at least 20 nucleotides long.

Other techniques for amplifying the target nucleic acid may be advantageously used as alternatives to PCR.

The nucleotide sequences of the invention, in particular the primers according to the

invention, may also be used in other methods for amplifying a target nucleic acid, such as:

- the TAS (Transcription-based Amplification System) technique described by Kwoh et al. in 1989;
- the 3SR (Self-Sustained Sequence Replication) technique described by Guatelli et al. in 1990;
- 5 the NASBA (Nucleic Acid Sequence Based Amplification) technique described by Kievitis et al. in 1991;
 - the SDA (Strand Displacement Amplification) technique (Walker et al., 1992);
 - the TMA (Transcription Mediated Amplification) technique.

25

35

The polynucleotides of the invention may also be used in techniques for amplifying or for modifying the nucleic acid serving as probe, such as:

- the LCR (Ligase Chain Reaction) technique described by Landegren et al. in 1988 and perfected by Barany et al. in 1991, which uses a thermostable ligase;
- the RCR (Repair Chain Reaction) technique described by Segev in 1992;
- the CPR (Cycling Probe Reaction) technique described by Duck et al. in 1990;
- the Q-beta-replicase amplification technique described by Miele et al. in 1983 and perfected in particular by Chu et al. in 1986, Lizardi et al. in 1988, and then by Burg et al. as well as by Stone et al. in 1996.

The invention also relates to the nucleotide sequences of fragments which can be obtained by amplification with the aid of at least one primer according to the invention. The present invention encompasses both hybridization probes and primers. In general, the complementary probes should be of the length sufficient to form a stable hybrid complex with the target sequences. Primers, while complementary to the target sequences need not form stable hybridization complexes with the target sequences alone. Rather, primers form stable complexes with the target sequences in the presence of polymerase to permit extension of the primer.

In the case where the target polynucleotide to be detected is possibly an RNA, for example an mRNA, it will be possible to use, prior to the use of an amplification reaction with the aid of at least one primer according to the invention or to the use of a method of detection with the aid of at least one probe of the invention, a reverse transcriptase-type enzyme so as to obtain a cDNA from the RNA contained in the biological sample. The cDNA obtained will then serve as target for the primer(s) or the probe(s) used in the amplification or detection method according to the invention.

The detection probe will be chosen so that it hybridizes with the target sequence or the amplicon generated from the target sequence. Such a detection probe will advantageously have as sequence a sequence of at least 12 nucleotides, 15 nucleotides, in particular of at least 20 nucleotides, and preferably at least 100 nucleotides.

The invention also comprises the nucleotide sequences which can be used as probe or

WO 99/28475 PCT/IB98/01939

51

primer according to the invention, characterized in that they are labelled with a radioactive compound or with a nonradioactive compound.

The nonlabelled nucleotide sequences may be used directly as probes or primers; however, the sequences are generally labelled with a radioactive element (³²P, ³⁵S, ³H, ¹²⁵I) or with a nonradioactive molecule (biotin, acetylaminofluorene, digoxigenin, 5-bromo-deoxyuridine, fluorescein) so as to obtain probes which can be used in numerous applications.

Examples of nonradioactive labelling of nucleotide sequences are described, for example, in French patent No. 78,10975 or by Urdea et al. or by Sanchez-Pescador et al. in 1988.

In the latter case, one of the labelling methods described in patents FR-2 422 956 and FR-2 518 755 may also be used.

The invention also relates to the nucleotide sequences of fragments which can be obtained by hybridization with the aid of at least one probe according to the invention.

The hybridization technique may be performed in various ways (Matthews et al., 1988). The most common method consists in immobilizing the nucleic acid extracted from C. trachomatis cells on a support (such as nitrocellulose, nylon, polystyrene) and in incubating, under well-defined conditions, the target nucleic acid immobilized with the probe. After hybridization, the excess probe is removed and the hybrid molecules formed are detected by the appropriate method (measurement of the radioactivity, of the fluorescence or of the enzymatic activity linked to the probe).

The invention also comprises the nucleotide sequences according to the invention, characterized in that they are covalently or noncovalently immobilized on a support.

20

According to another advantageous embodiment of the nucleic sequences according to the invention, the latter may be used immobilized on a support and may thus serve to capture, through specific hybridization, the target nucleic acid obtained from the biological sample to be tested. If necessary, the solid support is separated from the sample and the hybridization complex formed between the so-called capture probe and the target nucleic acid is then detected by means of a second probe, called detection probe, labelled with an easily detectable element.

The nucleotide sequences according to the invention may also be used in new analytical systems, DNA chips, which allow sequencing, the study of mutations and of the expression of genes, and which are currently of interest given their very small size and their high capacity in terms of number of analyses.

The principle of the operation of these chips is based on molecular probes, most often oligonucleotides, which are attached onto a miniaturized surface, generally of the order of a few square centimetres. During an analysis, a sample containing fragments of a target nucleic acid to be analysed, for example DNA or RNA labelled, for example, after amplification, is deposited onto the

WO 99/28475

20

35

DNA chip in which the support has been coated beforehand with probes. Bringing the labelled target sequences into contact with the probes leads to the formation, through hybridization, of a duplex according to the rule of pairing defined by J.D. Watson and F. Crick. After a washing step, analysis of the surface of the chip allows the effective hybridizations to be located by means of the signals emitted by the labels tagging the target. A hybridization fingerprint results from this analysis which, by appropriate computer processing, will make it possible to determine information such as the presence of specific fragments in the sample, the determination of sequences and the presence of mutations.

The chip consists of a multitude of molecular probes, precisely organized or arrayed on a solid support whose surface is miniaturized. It is at the centre of a system where other elements (imaging system, microcomputer) allow the acquisition and interpretation of a hybridization fingerprint.

The hybridization supports are provided in the form of flat or porous surfaces (pierced with wells) composed of various materials. The choice of a support is determined by its physicochemical properties, or more precisely, by the relationship between the latter and the conditions under which the support will be placed during the synthesis or the attachment of the probes or during the use of the chip. It is therefore necessary, before considering the use of a particular support (R.S. Matson et al., 1994), to consider characteristics such as its stability to pH, its physical strength, its reactivity and its chemical stability as well as its capacity to nonspecifically bind nucleic acids. Materials such as glass, silicon and polymers are commonly used. Their surface is, in a first step, called «functionalization», made reactive towards the groups which it is desired to attach thereon. After the functionalization, so-called spacer molecules are grafted onto the activated surface. Used as intermediates between the surface and the probe, these molecules of variable size render unimportant the surface properties of the supports, which often prove to be problematic for the synthesis or the attachment of the probes and for the hybridization.

Among the hybridization supports, there may be mentioned glass which is used, for example, in the method of in situ synthesis of oligonucleotides by photochemical addressing developed by the company Affymetrix (E.L. Sheldon, 1993), the glass surface being activated by silane. Genosensor Consortium (P. Mérel, 1994) also uses glass slides carrying wells 3 mm apart, this support being activated with epoxysilane.

Polymers or silicon may also be mentioned among these hybridization supports. For example, the Andrein Mirzabekov team has developed a chip consisting of polyacrylamide squares polymerized on a silanized glass surface (G. Yershov et al., 1996). Several teams use silicon, in particular the IFOS laboratory of Ecole Centrale of Lyon which uses a silicon semiconductor substrate which is p-doped by introducing it into its crystalline structure atoms whose valency is different from

WO 99/28475 PCT/IB98/01939

53

that of silicon. Various types of metals, in particular gold and platinum, may also be used as support (Genosensor Consortium (K. Beattie et al., 1993)).

The probes according to the invention may be synthesized directly in situ on the supports of the DNA chips. This in situ synthesis may be carried out by photochemical addressing (developed by the company Affymax (Amsterdam, Holland) and exploited industrially by its subsidiary Affymetrix (United States)) or based on the VLSIPS (very large scale immobilized polymer synthesis) technology (S.P.A. Fodor et al., 1991) which is based on a method of photochemically directed combinatory synthesis and the principle of which combines solid-phase chemistry, the use of photolabile protecting groups and photolithography.

The probes according to the invention may be attached to the DNA chips in various ways such as electrochemical addressing, automated addressing or the use of probe printers (T. Livache et al., 1994; G. Yershov et al., 1996; J. Derisi et al., 1996, and S. Borman, 1996).

10

15

20

The revealing of the hybridization between the probes of the invention, deposited or synthesized in situ on the supports of the DNA chips, and the sample to be analysed, may be determined, for example, by measurement of fluorescent signals, by radioactive counting or by electronic detection.

The use of fluorescent molecules such as fluorescein constitutes the most common method of labelling the samples. It allows direct or indirect revealing of the hybridization and allows the use of various fluorochromes.

Affymetrix currently provides an apparatus or a scanner designed to read its Gene Chip? chips. It makes it possible to detect the hybridizations by scanning the surface of the chip in confocal microscopy (R.J. Lipshutz et al., 1995). Other methods of detecting fluorescent signals have been tested: coupling of an epifluorescence microscope and a CCD camera (G. Yershov et al., 1996), the use of an optical fibre collecting system (E.L. Sheldon, 1993). A conventional method consists in carrying out an end labelling, with phosphorus 32, of the target sequences, by means of an appropriate apparatus, the Phosphorimager (marketed by Molecular Dynamics). The electronic detection is based on the principle that the hybridization of two nucleic acid molecules is accompanied by physical phenomena which can be quantified under certain conditions (system developed by Ecole Centrale of Lyon and called GEN-FET (GEN field effect transistor)). Genosensor Consortium and the company Beckman Instruments who are developing an electronic chip or Permittivity Chips? may also be mentioned (K. Beattie et al., 1993).

The nucleotide sequences according to the invention may thus be used in DNA chips to carry out the analysis of mutations. This analysis is based on the production of chips capable of analysing each base of a nucleotide sequence according to the invention. It is possible, in particular to this end, to use the microsequencing techniques on a DNA chip. The mutations are detected by

extending immobilized primers which hybridize to the template of sequences analysed, just at the position adjacent to that of the mutated nucleotide to be detected. A single-stranded template, RNA or DNA, of the sequences to be analysed will be advantageously prepared according to conventional methods, from products amplified according to PCR-type techniques. The templates of single-stranded DNA, or of RNA thus obtained are then deposited on the DNA chip, under conditions allowing their specific hybridization to the immobilized primers. A thermostable polymerase, for example Tth or T7 DNA polymerase, specifically extends the 3' end of the immobilized primer with a labelled nucleotide analogue complementary to the nucleotide at the position of the variable site. For example a thermal cycling is performed in the presence of fluorescent dideoxyribonucleotides.

The experimental conditions will be adapted in particular to the chips used, to the immobilized primers, to the polymerases used and to the labelling system chosen. One advantage of microsequencing, compared with techniques based on the hybridization of probes, is that it makes it possible to identify all the variable nucleotides with optimal discrimination under homogeneous reaction conditions; used on DNA chips, it allows optimal resolution and specificity for the routine and industrial detection of mutations in multiplex.

The nucleotide sequences according to the invention may also be used in DNA chips to carry out the analysis of the expression of the *Chlamydia trachomatis* genes. This analysis of the expression of *Chlamydia trachomatis* genes is based on the use of chips where probes of the invention, chosen for their specificity to characterize a given gene, are present (D.J. Lockhart et al., 1996; D.D. Shoemaker et al., 1996). For the methods of analysis of gene expression using the DNA chips, reference may, for example, be made to the methods described by D.J. Lockhart et al. (1996) and Sosnowsky et al. (1997) for the synthesis of probes in situ or for the addressing and the attachment of previously synthesized probes. The target sequences to be analysed are labelled and in general fragmented into sequences of about 50 to 100 nucleotides before being hybridized onto the chip. After washing as described, for example, by D.J. Lockhart et al. (1996) and application of different electric fields (Sosnowsky et al., 1997), the labelled compounds are detected and quantified, the hybridizations being carried out at least in duplicate. Comparative analyses of the signal intensities obtained with respect to the same probe for different samples and/or for different probes with the same sample, determine the differential expression of RNA or of DNA derived from the sample.

The nucleotide sequences according to the invention may, in addition, be used in DNA chips where other nucleotide probes specific for other microorganisms are also present, and may allow the carrying out of a serial test allowing rapid identification of the presence of a microorganism in a sample.

30

WO 99/28475 PCT/IB98/01939

55

to the invention, characterized in that they are immobilized on a support of a DNA chip.

5

10

20

25

35

The DNA chips, characterized in that they contain at least one nucleotide sequence according to the invention, immobilized on the support of the said chip, also form part of the invention.

The said chips will preferably contain several probes or nucleotide sequences of the invention of different length and/or corresponding to different genes so as to identify, with greater certainty, the specificity of the target sequences or the desired mutation in the sample to be analysed.

Accordingly, the analyses carried out by means of primers and/or probes according to the invention, immobilized on supports such as DNA chips, will make it possible, for example, to identify, in samples, mutations linked to variations such as intraspecies variations. These variations may be correlated or associated with pathologies specific to the variant identified and will make it possible to select the appropriate treatment.

The invention thus comprises a DNA chip according to the invention, characterized in that it contains, in addition, at least one nucleotide sequence of a microorganism different from
15 Chlamydia trachomatis, immobilized on the support of the said chip; preferably, the different microorganism will be chosen from an associated microorganism, a bacterium of the Chlamydia family, and a variant of the species Chlamydia trachomatis.

Another subject of the present invention is a vector for the cloning and/or the expression of a sequence, characterized in that it contains a nucleotide sequence according to the invention.

Among the said vectors according to the invention, the vectors containing a nucleotide sequence encoding a polypeptide of the cellular, preferably outer, envelope of *Chlamydia trachomatis* or one of its representative fragments, are preferred.

In a specific embodiment, the vectors contain a nucleotide sequence encoding a Chlamydia trachomatis secreted polypeptide or one of its representative fragments or encoding a transport polypeptide, a surface exposed polypeptide, a lipoprotein or one of its representative fragments, a polypeptide involved in lipopolysaccharide (LPS) biosynthesis, a Type III or non-Type III secreted polypeptide, a polypeptide containing RGD attachment sites, a cell wall anchored surface polypeptide, a polypeptide not found in Chlamydia pneumoniae, a ribosomal polypeptide or a polypeptide involved in secretion, transcription, translation, maturation of proteins, a polypeptide involved in the synthesis of the wall, a polypeptide involved in the virulence, a polypeptide involved in the intermediate metabolism, in particular in the metabolism of sugars and/or of cofactors, a polypeptide involved in the metabolism of nucleotides, of amino acids, of nucleic acids or of fatty acids of Chlamydia trachomatis or one of their representative fragments, or a polypeptide specific to Chlamydiae, are also preferred.

According to the invention, the vectors comprise the elements necessary to allow the expression and/or the secretion of the said nucleotide sequences in a given host cell, and also form part of the invention.

The vector should, in this case, comprise a promoter, signals for initiation and for termination of translation, as well as appropriate regions for regulation of transcription. It should be capable of being stably maintained in the host cell and may optionally possess particular signals specifying the secretion of the translated protein. These different elements are chosen according to the host cell used. To this effect, the nucleotide sequences according to the invention may be inserted into autonomously-replicating vectors within the chosen host, or integrative vectors in the chosen host.

Any of the standard methods known to those skilled in the art for the insertion of DNA fragments into a vector may be used to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and the protein coding sequences. These methods may include *in vitro* recombinant DNA and synthetic techniques and *in vivo* recombinants (genetic recombination).

10

15

Expression of a polypeptide, peptide or derivative, or analogs thereof encoded by a polynucleotide sequence in SEQ ID No. 1 or ORFs contained within SEQ ID No. 1 may be regulated by a second nucleic acid sequence so that the protein or peptide is expressed in a host transformed with the recombinant DNA molecule. For example, expression of a protein or peptide may be controlled by any promoter/enhancer element known in the art. Promoters which may be used to control expression include, but are not limited to, the CMV promoter, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto, et al., 1980, Cell 22:787-797), the herpes thymidine kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. U.S.A. 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, Nature 296:39-42); prokaryotic expression vectors such as the B-lactamase promoter (Villa-Kamaroff, et al., 1978, Proc. Natl. Acad. Sci. U.S.A. 75:3727-3731), or the tac promoter (DeBoer, et al., 1983, Proc. Natl. Acad. Sci. U.S.A. 80:21-25); see also "Useful proteins from recombinant bacteria" in Scientific American, 1980, 242:74-94; plant expression vectors comprising the nopaline synthetase promoter region (Herrera-Estrella et al., 1983, Nature 303:209-213) or the cauliflower mosaic virus 35S RNA promoter (Gardner, et al., 1981, Nucl. Acids Res. 9:2871), and the promoter of the photosynthetic enzyme ribulose biphosphate carboxylase (Herrera-Estrella et al., 1984, Nature 310:115-120); promoter elements from yeast or other fungi such as the Gal 4 promoter, the ADC (alcohol dehydrogenase) promoter, PGK (phosphoglycerol kinase) promoter, alkaline phosphatase promoter, and the following animal transcriptional control regions, which exhibit tissue specificity and have been utilized in transgenic animals: elastase I gene control region which is active in pancreatic acinar cells (Swift et al., 1984, Cell 38:639-646; Ornitz et al., WO 99/28475 PCT/IB98/01939

57

1986, Cold Spring Harbor Symp. Quant. Biol. 50:399-409; MacDonald, 1987, Hepatology 7:425-515); insulin gene control region which is active in pancreatic beta cells (Hanahan, 1985, Nature 315:115-122), immunoglobulin gene control region which is active in lymphoid cells (Grosschedl et al., 1984, Cell 38:647-658; Adames et al., 1985, Nature 318:533-538; Alexander et al., 1987, Mol. Cell. Biol. 7:1436-1444), mouse mammary tumor virus control region which is active in testicular, breast, lymphoid and mast cells (Leder et al., 1986, Cell 45:485-495), albumin gene control region which is active in liver (Pinkert et al., 1987, Genes and Devel. 1:268-276), alpha-fetoprotein gene control region which is active in liver (Krumlauf et al., 1985, Mol. Cell. Biol. 5:1639-1648; Hammer et al., 1987, Science 235:53-58; alpha 1-antitrypsin gene control region which is active in the liver

myeloid cells (Mogram et al., 1985, Nature 315:338-340; Kollias et al., 1986, Cell 46:89-94; myelin basic protein gene control region which is active in oligodendrocyte cells in the brain (Readhead et al., 1987, Cell 48:703-712); myosin light chain-2 gene control region which is active in skeletal muscle (Sani, 1985, Nature 314:283-286), and gonadotropic releasing hormone gene control region

(Kelsey et al., 1987, Genes and Devel. 1:161-171), beta-globin gene control region which is active in

which is active in the hypothalamus (Mason et al., 1986, Science 234:1372-1378).

20

25

30

35

The vectors according to the invention are, for example, vectors of plasmid or viral origin. In a specific embodiment, a vector is used that comprises a promoter operably linked to a protein or peptide-encoding nucleic acid sequence in SEQ ID No. 1, or ORFs contained within SEQ ID No. 1, one or more origins of replication, and, optionally, one or more selectable markers (e.g., an antibiotic resistance gene). Expression vectors comprise regulatory sequences that control gene expression, including gene expression in a desired host cell. Preferred vectors for the expression of the polypeptides of the invention include the pET-type plasmid vectors (Promega) or pBAD plasmid vectors (Invitrogen). Furthermore, the vectors according to the invention are useful for transforming host cells so as to clone or express the nucleotide sequences of the invention.

Expression can also be achieved using targeted homologous recombination to activate Chlamydia trachomatis genes present in the cloned genomic DNA. A heterologous regulatory element may be inserted into a stable cell line or cloned microorganism, such that it is operatively linked with an endogenous Chlamydia trachomatis gene present in the cloned genome, using techniques, such as targeted homologous recombination, which are well known to those of skill in the art (See, e.g., Chappel, U.S. Patent No. 4,215,051 and Skoultchi, WO 91/06667 each of which is incorporated herein in its entirety).

Expression vector/host cell systems containing inserts of polynucleotide sequences in SEQ ID No. 1 or ORFs within SEQ ID No. 1, which encode polypeptides, peptides or derivatives, or analogs thereof, can be identified by three general approaches: (a) nucleic acid hybridization, (b) presence or absence of "marker" gene functions, and (c) expression of inserted sequences. In the first

approach, the presence of a polynucleotide sequence inserted in an expression vector can be detected by nucleic acid hybridization using probes comprising sequences that are homologous to an inserted polynucleotide sequence. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "marker" gene functions (e.g., thymidine kinase activity, resistance to antibiotics, transformation phenotype, occlusion body formation in baculovirus, etc.) caused by the insertion of a polynucleotide sequence in the vector. For example, if the polynucleotide sequence in SEQ ID No. 1 or ORFs within SEQ ID No. 1 is inserted within the marker gene sequence of the vector, recombinants containing the insert can be identified by the absence of the marker gene function. In the third approach, recombinant expression vectors can be identified by assaying the product of the polynucleotide sequence expressed by the recombinant. Such assays can be based, for example, on the physical or functional properties of the expressed polypeptide in in vitro assay systems, e.g., binding with antibody, promotion of cell proliferation.

Once a particular recombinant DNA molecule is identified and isolated, several methods known in the art may be used to propagate it. The clones identified may be introduced into an appropriate host cell by standard methods, such as for example lipofection, electroporation, and heat shock. Once a suitable host system and growth conditions are established, recombinant expression vectors can be propagated and prepared in quantity.

The invention also encompasses the host cells transformed by a vector according to the invention. These cells may be obtained by introducing into host cells a nucleotide sequence inserted into a vector as defined above, and then culturing the said cells under conditions allowing the replication and/or the expression of the transfected nucleotide sequence.

The host cell may be chosen from eukaryotic or prokaryotic systems, such as for example bacterial cells (Olins and Lee, 1993), but also yeast cells (Buckholz, 1993), as well as animal cells, in particular cultures of mammalian cells (Edwards and Aruffo, 1993), and in particular Chinese hamster ovary (CHO) cells, but also insect cells in which methods using baculoviruses for example may be used (Luckow, 1993).

Furthermore, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus, expression of the genetically engineered polypeptide may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation) of proteins. Appropriate cell lines or host systems can be chosen to ensure the desired modification and processing of the foreign protein expressed. For example, expression in a bacterial system can be used to produce an unglycosylated core protein product. Expression in yeast will produce a glycosylated product. Expression in

20

25

mammalian cells can be used to ensure "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

A preferred host cell for the expression of the proteins of the invention consists of prokaryotic cells, such as Gram negative bacteria.

A further preferred host cell according to the invention is a bacterium belonging to the *Chlamydia* family, more preferably belonging to the species *Chlamydia trachomatis* or chosen from a microorganism associated with the species *Chlamydia trachomatis*.

In other specific embodiments, the polypeptides, peptides or derivatives, or analogs thereof may be expressed as a fusion, or chimeric protein product (comprising the protein, fragment, analog, or derivative joined via a peptide bond to a heterologous protein sequence (of a different protein)). Such a chimeric product can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acid sequences to each other by methods known in the art, in the proper coding frame, and expressing the chimeric product by methods commonly known in the art. Alternatively, such a chimeric product may be made by protein synthetic techniques, *e.g.*, by use of a peptide synthesizer.

Genomic sequences can be cloned and expressed as translational gene products (i.e., peptides, polypeptides, and proteins) or transcriptional gene products (i.e., antisense and ribozymes).

The invention further relates to the intracellular production of an antisense nucleic acid sequence of SEQ ID No. 1 by transcription from an exogenous sequence. For example, a vector can be introduced *in vivo* such that it is taken up by a cell, within which cell the vector or a portion thereof is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding an antisense nucleic acid. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art, used for replication and expression in mammalian cells. Expression of the sequence encoding the antisense RNA can be by any promoter known in the art to act in mammalian, preferably human, cells. Such promoters can be inducible or constitutive. Such promoters include but are not limited to: the CMV promoter, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3N long terminal repeat of Rous sarcoma virus (Yamamoto *et al.*, 1980, Cell 22:787-797), the herpes thymidine kinase promoter (Wagner *et al.*, 1981, Proc. Natl. Acad. Sci. U.S.A. 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster *et al.*, 1982, Nature 296:39-42), etc.

In a specific embodiment, the antisense oligonucleotide comprises catalytic RNA, or a ribozyme (see, e.g., PCT International Publication WO 90/11364, published October 4, 1990; Sarver et al., 1990, Science 247:1222-1225). In another embodiment, the oligonucleotide is a 2N-0-

25

30

methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analog (Inoue et al., 1987, FEBS Lett. 215:327-330).

In another embodiment, the antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a polynucleotide sequence in SEQ ID No. 1. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," as referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acid sequence, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with an RNA transcribed from SEQ ID No. 1 may contain and still form a stable duplex (or triplex, as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

The invention also relates to the animals, except humans, comprising one of the above-described transformed cells according to the invention.

The production of transgenic animals according to the invention overexpressing one or more of the *Chlamydia trachomatis* genes will be preferably carried out on rats, mice or rabbits according to methods well known to persons skilled in the art such as viral or nonviral transfections. The transgenic animals overexpressing one or more of the said genes may be obtained by transfection of multiple copies of the said genes under the control of a powerful promoter of a ubiquitous nature, or which is selective for one type of tissue. The transgenic animals may also be obtained by homologous recombination on embryonic stem cells, transfer of these stem cells to embryos, selection of the chimeras affected at the level of the reproductive lines, and growth of the said chimeras.

The transformed cells as well as the transgenic animals according to the invention can be used in methods of preparing the recombinant polypeptide.

It is now possible to produce recombinant polypeptides in a relatively large quantity by genetic engineering using the cells transformed with expression vectors according to the invention or using transgenic animals according to the invention.

The methods of preparing a polypeptide of the invention in recombinant form, characterized in that they use a vector and/or a cell transformed with a vector according to the invention and/or a transgenic animal comprising one of the said transformed cells according to the invention, are themselves included in the present invention.

Among the said methods of preparing a polypeptide of the invention in recombinant form, the methods of preparation using a vector, and/or a cell transformed with the said vector and/or

25

a transgenic animal comprising one of the said transformed cells, containing a nucleotide sequence encoding a polypeptide of the cellular envelope of Chlamydia trachomatis or one of its representative fragments, more preferably encoding a polypeptide of the outer cellular envelope of Chlamydia trachomatis or one of its fragment, are preferred.

Among the said methods of preparing a polypeptide of the invention in recombinant form, the methods of preparation using a vector, and/or a cell transformed with the said vector and/or a transgenic animal comprising one of the said transformed cells, containing a nucleotide sequence encoding a Chlamydia trachomatis secreted polypeptide or one of its representative fragments, or encoding a transport polypeptide, a surface exposed polypeptide, a lipoprotein or one of its representative fragments, a polypeptide involved in lipopolysaccharide biosynthesis, a Type III or other secreted polypeptide, a polypeptide containing RGD attachment sites, a cell wall anchored surface polypeptide, a polypeptide not found in Chlamydia pneumoniae, a ribosomal polypeptide or a polypeptide involved in secretion, transcription, translation, maturation of proteins, a polypeptide involved in the synthesis of the wall, a polypeptide involved in the virulence, a polypeptide involved 15 in the intermediate metabolism, in particular in the metabolism of sugars and/or of cofactors, a polypeptide involved in the metabolism of nucleotides, of amino acids, of nucleic acids or of fatty acids of Chlamydia trachomatis or one of their representative fragments, or a polypeptide specific to Chlamydiae, are also preferred.

The recombinant polypeptides obtained as indicated above may be provided either in glycosylated or nonglycosylated form and may or may not have the natural tertiary structure. 20

A preferred variant consists in producing a recombinant polypeptide fused to a «carrier» protein (chimeric protein). The advantage of this system is that it allows a stabilization and a reduction in proteolysis of the recombinant product, an increase in solubility during renaturation in vitro and/or a simplification of purification when the fusion partner has affinity for a specific ligand.

More particularly, the invention relates to a method of preparing a polypeptide of the invention comprising the following steps:

- a) culture of the transformed cells under conditions allowing the expression of a recombinant polypeptide having a nucleic acid sequence according to the invention;
- 30 b) where appropriate, recovery of the said recombinant polypeptide.

When the method of preparing a polypeptide of the invention uses a transgenic animal according to the invention, the recombinant polypeptide is then extracted from the said animal.

The subject of the invention is also a polypeptide capable of being obtained by a method of the invention as described above.

35 The invention also comprises a method of preparing a synthetic polypeptide,

20

30

characterized in that it uses an amino acid sequence of polypeptides according to the invention.

The invention also relates to a synthetic polypeptide obtained by a method according to the invention.

Polypeptides according to the invention may also be prepared by conventional techniques in the field of peptide synthesis under conditions suitable to produce the polypeptides encoded by the polynucleotide of the invention. This synthesis may be carried out in and recovered from a homogeneous solution or on a solid phase.

For example, the synthesis technique in a homogeneous solution described by Houbenweyl in 1974 may be used.

This method of synthesis consists in successively condensing, in pairs, the successive amino acids in the required order, or in condensing amino acids and fragments previously formed and already containing several amino acids in the appropriate order, or alternatively several fragments thus previously prepared, it being understood that care will have been taken to protect beforehand all the reactive functional groups carried by these amino acids or fragments, with the exception of the amine functional groups of one and the carboxyl functional groups of the other or vice versa, which should normally take part in the formation of the peptide bonds, in particular after activation of the carboxyl functional group, according to methods well known in peptide synthesis.

According to another preferred technique of the invention, the one described by Merrifield is used.

To manufacture a peptide chain according to the Merrifield method, a highly porous polymer resin is used, onto which the first C-terminal amino acid of the chain is attached. This amino acid is attached onto a resin via its carboxyl group and its amine functional group is protected. The amino acids which will constitute the peptide chain are thus attached, one after another, onto the amine group, each time deprotected beforehand, of the portion of the peptide chain already formed, and which is attached to the resin. When the entire peptide chain desired is formed, the protecting groups are removed from the various amino acids constituting the peptide chain and the peptide is detached from the resin with the aid of an acid.

The invention relates, in addition, to hybrid (fusion) polypeptides having at least one polypeptide or one of its representative fragments according to the invention, and a sequence of a polypeptide capable of eliciting an immune response in humans or animals.

Advantageously, the antigenic determinant is such that it is capable of eliciting a humoral and/or cellular response.

An antigenic determinant may be identified by screening expression libraries of the Chlamydia trachomatis genome with antibodies contained in the serum of patients infected with a bacterium belonging to the species Chlamydia trachomatis. An antigenic determinant may comprise a

WO 99/28475 PCT/IB98/01939

63

polypeptide or one of its fragments according to the invention, in glycosylated form, used in order to obtain immunogenic compositions capable of inducing the synthesis of antibodies directed against multiple epitopes. The said polypeptides or their glycosylated fragments also form part of the invention.

These hybrid molecules may consist, in part, of a carrier molecule for polypeptides or for their representative fragments according to the invention, combined with a portion which may be immunogenic, in particular an epitope of the diphtheria toxin, the tetanus toxin, a hepatitis B virus surface antigen (patent FR 79 21811), the poliomyelitis virus VP1 antigen or any other viral or bacterial toxin or antigen.

5

10

The methods of synthesizing the hybrid molecules include the methods used in genetic engineering to construct hybrid nucleotide sequences encoding the desired polypeptide sequences. Reference may be advantageously made, for example, to the technique for producing genes encoding fusion proteins described by Minton in 1984.

The said hybrid nucleotide sequences encoding a hybrid polypeptide as well as the hybrid polypeptides according to the invention, characterized in that they are recombinant polypeptides obtained by the expression of the said hybrid nucleotide sequences, also form part of the invention.

The invention also comprises the vectors characterized in that they contain one of the said hybrid nucleotide sequences. The host cells transformed by the said vectors, the transgenic animals comprising one of the said transformed cells as well as the methods of preparing recombinant polypeptides using the said vectors, the said transformed cells and/or the said transgenic animals of course also form part of the invention.

The polypeptides according to the invention, the antibodies according to the invention described below and the nucleotide sequences according to the invention may advantageously be used in *in vitro* and/or *in vivo* methods for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis*, in a biological sample (biological tissue or fluid) which is likely to contain them. These methods, depending on the specificity of the polypeptides, of the antibodies and of the nucleotide sequences according to the invention which will be used, may in particular detect and/or identify the bacterial variants belonging to the species *Chlamydia trachomatis* as well as the associated microorganisms capable of being detected by the polypeptides, the antibodies and the nucleotide sequences according to the invention which will be chosen. It may, for example, be advantageous to choose a polypeptide, an antibody or a nucleotide sequence according to the invention, which is capable of detecting any bacterium of the *Chlamydia* family by choosing a polypeptide, an antibody and/or a nucleotide sequence according to the invention which is specific to the family or, on the contrary, it will be most particularly advantageous to target a variant of the

species Chlamydia trachomatis, which is responsible, for example, for the induction or the worsening of pathologies specific to the targeted variant, by choosing a polypeptide, an antibody and/or a nucleotide sequence according to the invention which is specific to the said variant.

The polypeptides according to the invention may advantageously be used in a method for the detection and/or the identification of bacteria belonging to the species Chlamydia trachomatis or to an associated microorganism, in a biological sample (biological tissue or fluid) which is likely to contain them, characterized in that it comprises the following steps:

- bringing this biological sample into contact with a polypeptide or one of its representative fragments according to the invention (under conditions allowing an immunological reaction between the said polypeptide and the antibodies which may be present in the biological sample);
 - detecting the antigen-antibody complexes which may be formed. b)

Preferably, the biological sample consists of a fluid, for example a human or animal serum, blood or biopsies.

Any conventional procedure may be used to carry out such a detection of the antigenantibody complexes which may be formed. 15

By way of example, a preferred method uses immunoenzymatic procedures based on the ELISA technique, immunofluorescence procedures or radioimmunological procedures (RIA), and the like.

Accordingly, the invention also relates to the polypeptides according to the invention, labelled with the aid of a suitable label such as a label of the enzymatic, fluorescent or radioactive 20 type.

Such methods comprise, for example, the following steps:

- deposition of defined quantities of a polypeptide composition according to the invention into the wells of a microtitre plate,
- introduction, into the said wells, of increasing dilutions of serum, or of a different biological 25 sample as defined above, which has to be analysed,
 - incubation of the microplate,

35

- introduction, into the wells of the microtitre plate, of labelled antibodies directed against human or animal immunoglobulins, these antibodies having been labelled with the aid of an enzyme selected from those which are capable of hydrolyzing a substrate, thereby modifying the absorption of the radiation of the latter, at least at a defined wavelength, for example at 550 nm,
- detection, by comparison with a control, of the quantity of substrate hydrolyzed.

The invention also relates to a kit or set for the detection and/or the identification of bacteria belonging to the species Chlamydia trachomatis or to an associated microorganism, characterized in that it comprises the following components:

a polypeptide according to the invention,

25

- where appropriate, the reagents for constituting the medium appropriate for the immunological or specific reaction,

65

- the reagents allowing the detection of the antigen-antibody complexes produced by the immunological reaction between the polypeptide(s) of the invention and the antibodies which may be present in the biological sample, it being possible for these reagents also to carry a label, or to be capable of being recognized in turn by a labelled reagent, more particularly in the case where the polypeptide according to the invention is not labelled,
- where appropriate, a reference biological sample (negative control) free of antibodies recognized by a polypeptide according to the invention,
 - where appropriate, a reference biological sample (positive control) containing a predetermined quantity of antibodies recognized by a polypeptide according to the invention.

According to the invention, the polypeptides, peptides, fusion proteins or other derivatives, or analogs thereof encoded by a polynucleotide sequence in SEQ ID No. 1, may be used as an immunogen to generate antibodies which immunospecifically bind such an immunogen. Such antibodies may include, but are not limited to, polyclonal and monoclonal antibodies, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab)₂ fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above. In a specific embodiment, the antibody to a polypeptide, peptide or other derivative, or analog thereof encoded by a polynucleotide sequence in SEQ ID No. 1 is a bispecific antibody (see generally, e.g. Fanger and Drakeman, 1995, Drug News and Perspectives 8: 133-137). Such a bispecific antibody is genetically engineered to recognize both (1) an epitope and (2) one of a variety of "trigger" molecules, e.g. Fc receptors on myeloid cells, and CD3 and CD2 on T cells, that have been identified as being able to cause a cytotoxic T-cell to destroy a particular target. Such bispecific antibodies can be prepared either by chemical conjugation, hybridoma, or recombinant molecular biology techniques known to the skilled artisan.

Various procedures known in the art may be used for the production of polyclonal antibodies to a polypeptide, peptide or other derivative, or analog thereof encoded by a polynucleotide sequence in SEQ ID No. 1. For the production of antibody, various host animals can be immunized by injection with a polypeptide, or peptide or other derivative, or analog thereof, including but not limited to rabbits, mice, rats, etc. Various adjuvants, depending on the host species, may be used to increase the immunological response, including but not limited to Stimulon™ QS-21 (Aquila Biopharmaceuticals, Inc., Framingham, MA), MPL™ (3-O-deacylated monophosphoryl lipid A; RIBI ImmunoChem Research, Inc., Hamilton, MT), aluminum phosphate, IL-12 (Genetics Institute, Cambridge, MA), Freund's (complete and incomplete), mineral gels such as aluminum hydroxide,

surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, BCG (bacille Calmette-Guerin), and corynebacterium parvum. Alternatively, polyclonal antibodies may be prepared by purifying, on an affinity column onto which a polypeptide according to the invention has been previously attached, the antibodies contained in the serum of patients infected with a bacterium belonging to the species Chlamydia trachomatis.

For preparation of monoclonal antibodies directed toward a polypeptide, peptide or other derivative, or analog, any technique which provides for the production of antibody molecules by continuous cell lines in culture may be used. For example, the hybridoma technique originally developed by Kohler and Milstein (1975, Nature 256:495-497), as well as the trioma technique, the human B-cell hybridoma technique (Kozbor et al., 1983, Immunology Today 4:72), and the EBVhybridoma technique to produce human monoclonal antibodies (Cole et al., 1985, in Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc., pp. 77-96). In an additional embodiment of the invention, monoclonal antibodies can be produced in germ-free animals utilizing technology described in PCT/US90/02545. In another embodiment of the invention, transgenic non-human animals can be used for the production of human antibodies utilizing technology described in WO 98/24893 and WO 96/33735. According to the invention, human antibodies may be used and can be obtained by using human hybridomas (Cote et al., 1983, Proc. Natl. Acad. Sci. U.S.A. 80:2026-2030) or by transforming human B cells with EBV virus in vitro (Cole et al., 1985, in Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, pp. 77-96). In fact, according to the invention, 20 techniques developed for the production of «chimeric antibodies», (Morrison et al., 1984, PROC. NATL. ACAD. SCI. U.S.A. 81:6851-6855; Neuberger et al., 1984, Nature 312:604-608; Takeda et al., 1985, Nature 314:452-454) by splicing the genes from a mouse antibody molecule specific for a polypeptide, peptide or other derivative, or analog together with genes from a human antibody molecule of appropriate biological activity can be used; such antibodies are within the scope of this invention.

According to the invention, techniques described for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce polypeptide or peptide-specific single chain antibodies. An additional embodiment of the invention utilizes the techniques described for the construction of Fab expression libraries (Huse et al., 1989, Science 246:1275-1281) to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity for polypeptides, derivatives, or analogs.

Antibody fragments which contain the idiotype of the molecule can be generated by known techniques. For example, such fragments include but are not limited to: the F(ab')2 fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragments which can be

30

generated by reducing the disulfide bridges of the F(ab')₂ fragment, the Fab fragments which can be generated by treating the antibody molecule with papain and a reducing agent, and Fv fragments.

In addition, techniques have been developed for the production of chimerized (See, e.g., Boss, M. et al., U.S. Patent No. 4,816,397; and Cabilly, S. et al., U.S. Patent No. 5,585,089 each of which is incorporated herein by reference in its entirety) humanized antibodies (See, e.g., Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) An immunoglobulin light or heavy chain variable region consists of a "framework" region interrupted by three hypervariable regions, referred to as complementarily determining regions (CDRs). The extent of the framework region and CDRs have been precisely defined (See, "Sequences of Proteins of Immunological Interest", Kabat, E. et al., U.S. Department of Health and Human Services (1983)). Briefly, humanized antibodies are antibody molecules from non-human species having one or more CDRs from the non-human species and a framework from a human immunoglobulin molecule.

The antibodies of the invention may also be labelled in the same manner as described above for the nucleic probes of the invention such as an enzymatic, fluorescent or radioactive type labelling.

The invention relates, in addition, to a method for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism in a biological sample, characterized in that it comprises the following steps:

- a) bringing the biological sample (biological tissue or fluid) into contact with a mono- or polyclonal antibody according to the invention (under conditions allowing an immunological reaction between the said antibodies and the polypeptides of the bacterium belonging to the species *Chlamydia trachomatis* or to an associated microorganism which may be present in the biological sample, that is, under conditions suitable for the formation of immune complexes);
 - b) detecting the antigen-antibody complex which may be formed.
- Also falling within the scope of the invention is a kit or set for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism, characterized in that it comprises the following components:
 - a polyclonal or monoclonal antibody according to the invention, labelled where appropriate;
 - where appropriate, a reagent for constituting the medium appropriate for carrying out the immunological reaction;
 - a reagent allowing the detection of the antigen-antibody complexes produced by the immunological reaction, it being possible for this reagent also to carry a label, or to be capable of being recognized in turn by a labelled reagent, more particularly in the case where the said monoclonal or polyclonal antibody is not labelled;
- 35 where appropriate, reagents for carrying out the lysis of the cells in the sample tested.

20

25

The principle of the DNA chip which was explained above may also be used to produce protein "chips" on which the support has been coated with a polypeptide or an antibody according to the invention, or arrays thereof, in place of the DNA. These protein "chips" make it possible, for example, to analyse the biomolecular interactions (BIA) induced by the affinity capture of target analytes onto a support coated, for example, with proteins, by surface plasma resonance (SPR). Reference may be made, for example, to the techniques for coupling proteins onto a solid support which are described in EP 524 800 or to the methods describing the use of biosensor-type protein chips such as the BIAcore-type technique (Pharmacia) (Arlinghaus et al., 1997, Krone et al., 1997, Chatelier et al., 1995). These polypeptides or antibodies according to the invention, capable of specifically binding antibodies or polypeptides derived from the sample to be analysed, may thus be used in protein chips for the detection and/or the identification of proteins in samples. The said protein chips may in particular be used for infectious diagnosis and may preferably contain, per chip, several polypeptides and/or antibodies of the invention of different specificity, and/or polypeptides and/or antibodies capable of recognizing microorganisms different from *Chlamydia trachomatis*.

Accordingly, the subject of the present invention is also the polypeptides and the antibodies according to the invention, characterized in that they are immobilized on a support, in particular of a protein chip.

The protein chips, characterized in that they contain at least one polypeptide or one antibody according to the invention immobilized on the support of the said chip, also form part of the invention.

The invention comprises, in addition, a protein chip according to the invention, characterized in that it contains, in addition, at least one polypeptide of a microorganism different from *Chlamydia trachomatis* or at least one antibody directed against a compound of a microorganism different from *Chlamydia trachomatis*, immobilized on the support of the said chip.

The invention also relates to a kit or set for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism, or for the detection and/or the identification of a microorganism characterized in that it comprises a protein chip according to the invention.

The subject of the present invention is also a method for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism in a biological sample, characterized in that it uses a nucleotide sequence according to the invention.

More particularly, the invention relates to a method for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism in a biological sample, characterized in that it comprises the following steps:

- a) where appropriate, isolation of the DNA from the biological sample to be analysed, or optionally production of a cDNA from the RNA in the biological sample;
- b) specific amplification of the DNA of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism with the aid of at least one primer according to the invention;
- 5 c) detection of the amplification products.

These may be detected, for example, by the molecular hybridization technique using a nucleic probe according to the invention. This probe will be advantageously labelled with a nonradioactive (cold probe) or radioactive element.

For the purposes of the present invention, "DNA in the biological sample" or "DNA contained in the biological sample" will be understood to mean either the DNA present in the biological sample considered, or optionally the cDNA obtained after the action of a reverse transcriptase-type enzyme on the RNA present in the said biological sample.

Another aim of the present invention consists in a method according to the invention, characterized in that it comprises the following steps:

- a) bringing a nucleotide probe according to the invention into contact with a biological sample, the DNA contained in the biological sample having, where appropriate, been previously made accessible to hybridization, under conditions allowing the hybridization of the probe to complementary base pairs of the DNA of a bacterium belonging to the species *Chlamydia trachomatis* or to an associated microorganism;
- b) detecting the hybridization complex formed between the nucleotide probe and the DNA in the biological sample.

The present invention also relates to a method according to the invention, characterized in that it comprises the following steps:

- a) bringing a nucleotide probe immobilized on a support according to the invention into contact with a biological sample, the DNA in the sample having, where appropriate, been previously made accessible to hybridization, under conditions allowing the hybridization of the probe to the DNA of a bacterium belonging to the species *Chlamydia trachomatis* or to an associated microorganism;
 - b) bringing the hybrid formed between the nucleotide probe immobilized on a support and the DNA contained in the biological sample, where appropriate after removal of the DNA in the biological sample which has not hybridized with the probe, into contact with a labelled nucleotide probe according to the invention;
 - c) detecting the new hybrid formed in step b).

According to an advantageous embodiment of the method for the detection and/or the identification defined above, it is characterized in that, prior to step a), the DNA in the biological sample is primer-extended and/or amplified beforehand with the aid of at least one primer according

to the invention.

35

The invention relates, in addition, to a kit or set for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism, characterized in that it comprises the following components:

- 5 a) a nucleotide probe according to the invention;
 - b) where appropriate, the reagents necessary for carrying out a hybridization reaction;
 - c) where appropriate, at least one primer according to the invention as well as the reagents (e.g., polymerase and/or deoxynucleotide triphosphates) necessary for a DNA amplification reaction.

The invention also relates to a kit or set for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism, characterized in that it comprises the following components:

- a) a nucleotide probe, called capture probe, according to the invention;
- b) an oligonucleotide probe, called detection probe, according to the invention;
- c) where appropriate, at least one primer according to the invention as well as the reagents (e.g., polymerase and/or deoxynucleotide triphosphates) necessary for a DNA amplification reaction.

The invention also relates to a kit or set for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism, characterized in that it comprises the following components:

- a) at least one primer according to the invention;
- 20 b) where appropriate, the reagents necessary for carrying out a DNA amplification reaction;
 - c) where appropriate, a component which makes it possible to check the sequence of the amplified fragment, more particularly an oligonucleotide probe according to the invention.

The invention relates, in addition, to a kit or set for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis* or to an associated microorganism, or for the detection and/or the identification of a microorganism characterized in that it comprises a DNA chip according to the invention.

The invention also relates to a method or to a kit or set according to the invention for the detection and/or the identification of bacteria belonging to the species *Chlamydia trachomatis*, characterized in that the said primer and/or the said probe according to the invention are chosen from the nucleotide sequences specific to the species *Chlamydia trachomatis*, in that the said polypeptides according to the invention are chosen from the polypeptides specific to the species *Chlamydia trachomatis* and in that the said antibodies according to the invention are chosen from the antibodies directed against the polypeptides according to the invention chosen from the polypeptides specific to the species *Chlamydia trachomatis*.

Preferably, the said method or the said kit or set above according to the invention, for

20

30

the detection and/or the identification of bacteria belonging to the species Chlamydia trachomatis is characterized in that the said primer and/or the said probe or the said polypeptides are chosen from the nucleotide sequences or polypeptides according to the invention which have been identified as being specific to the species Chlamydia trachomatis and in that the said antibodies according to the invention are chosen from the antibodies directed against the polypeptides according to the invention chosen from the polypeptides identified as being specific to the species Chlamydia trachomatis.

The invention relates, in addition, to a method or a kit or set according to the invention for the diagnosis of predispositions to, or of a condition caused by, genital diseases which are induced or worsened by a *Chlamydia trachomatis* infection.

The invention also relates to a method or a kit or set according to the invention for the diagnosis of predispositions to, or of conditions caused by, eye diseases induced or worsened by a *Chlamydia trachomatis* infection.

The invention also relates to a method or a kit or set according to the invention for the diagnosis of predispositions to, or of conditions caused by, systemic diseases, in particular of the lymphatic system, which are induced or worsened by a *Chlamydia trachomatis* infection.

According to another aspect, the subject of the invention is the use of polypeptides according to the invention, of cells transformed with a vector according to the invention and/or of transformed animals according to the invention, for the biosynthesis or the biodegradation of organic or inorganic compounds.

As has been mentioned above, the nucleotide sequences of the invention were identified by homology with sequences known to encode, for example, polypeptides or fragments of enzymatic polypeptides involved in the biosynthesis or the biodegradation of organic or inorganic molecules.

It is thus possible to use the said polypeptides of the invention in a similar manner for the biosynthesis or the biodegradation of organic or inorganic compounds of industrial or therapeutic interest (called compounds of interest).

Among these polypeptides, there may be mentioned in particular the enzymes involved in metabolism, such as the proteolytic enzymes, amino transferases, glucose metabolism, or the enzymes which may be used in the biosynthesis of sugars, amino acids, fatty acids, polypeptides, nucleotides, nucleic acids or any other organic or inorganic compound or in the biodegradation of organic or inorganic compounds.

Among these polypeptides, there may be mentioned, in addition, the mutated or modified enzymes corresponding to mutated or modified polypeptides according to the invention which may also be used for the biosynthesis or the biodegradation of organic or inorganic compounds at the industrial level, such as, for example, the production of compounds of interest, the reprocessing

of manufacturing residues applied to the food industries, to the papermaking industry or to the chemical and pharmaceutical industries.

The methods of biosynthesis or biodegradation of organic or inorganic compounds, characterized in that they use a polypeptide or one of its representative fragments according to the invention, transformed cells according to the invention and/or a transformed animal according to the invention, also form part of the invention.

The invention relates, in addition, to the use of a nucleotide sequence according to the invention, of a polypeptide according to the invention, of an antibody according to the invention, of a cell according to the invention, and/or of a transformed animal according to the invention, for the selection of an organic or inorganic compound capable of modulating, regulating, inducing or inhibiting the expression of genes, and/or of modifying the cellular replication of eukaryotic or prokaryotic cells or capable of inducing, inhibiting or worsening the pathologies linked to an infection by *Chlamydia trachomatis* or one of its associated microorganisms.

The invention also comprises screening assays that comprise method of selecting compounds capable of binding to a polypeptide, fusion polypeptide, or one of its representative fragments according to the invention, capable of binding to a nucleotide sequence according to the invention, or capable of recognizing an antibody according to the invention, and/or capable of modulating, regulating, inducing or inhibiting the expression of genes, and/or of modifying the growth or the cellular replication of eukaryotic or prokaryotic cells, or capable of inducing, inhibiting or worsening, in an animal or human organism, the pathologies linked to an infection by *Chlamydia trachomatis* or one of its associated microorganisms, characterized in that it comprises the following steps:

- a) bringing the said compound into contact with the said polypeptide, the said nucleotide sequence, with a transformed cell according to the invention and/or administering the said compound to a transformed animal according to the invention;
- b) determining the capacity of the said compound to bind with the said polypeptide or the said nucleotide sequence, or to modulate, regulate, induce or inhibit the expression of genes, or to modulate growth or cellular replication, or to induce, inhibit or worsen in the said transformed animal, the pathologies linked to an infection by *Chlamydia trachomatis* or one of its associated microorganisms.

The transformed cells and/or animals according to the invention may advantageously serve as a model and may be used in methods for studying, identifying and/or selecting compounds capable of being responsible for pathologies induced or worsened by *Chlamydia trachomatis*, or capable of preventing and/or of treating these pathologies such as, for example, genital, eye or systemic diseases, especially of the lymphatic system. In particular, the transformed host cells, in

WO 99/28475 PCT/IB98/01939

73

particular bacteria of the Chlamydia family whose transformation with a vector according to the invention may, for example, increase or inhibit its infectivity, or modulate the pathologies usually induced or worsened by the infection, may be used to infect animals in which the onset of pathologies will be monitored. These nontransformed animals, infected for example with transformed Chlamydia bacteria, may serve as a study model. In the same manner, the transformed animals according to the invention may, for example, exhibit predispositions to genital and/or eye and/or systemic diseases, especially of the lymphatic system, and thus be used in methods for selecting compounds capable of preventing and/or of treating the said diseases. The said methods using the said transformed cells and/or transformed animals form part of the invention.

The compounds capable of being selected may be organic compounds such as polypeptides or carbohydrates or any other organic or inorganic compounds already known, or new organic compounds produced using molecular modelling techniques and obtained by chemical or biochemical synthesis, these techniques being known to persons skilled in the art.

10

20

The said selected compounds may be used to modulate the growth and/or the cellular 15 replication of Chlamydia trachomatis or any other associated microorganism and thus to control infection by these microorganisms. The said compounds according to the invention may also be used to modulate the growth and/or the cellular replication of all eukaryotic or prokaryotic cells, in particular tumour cells and infectious microorganisms, for which the said compounds will prove active, the methods which make it possible to determine the said modulations being well known to persons skilled in the art.

Compound capable of modulating the growth of a microorganism is understood to designate any compound which makes it possible to act, to modify, to limit and/or to reduce the development, the growth, the rate of proliferation and/or the viability of the said microorganism.

This modulation may be achieved, for example, by an agent capable of binding to a protein and thus of inhibiting or of potentiating its biological activity, or capable of binding to a membrane protein of the outer surface of a microorganism and of blocking the penetration of the said microorganism into the host cell or of promoting the action of the immune system of the infected organism directed against the said microorganism. This modulation may also be achieved by an agent capable of binding to a nucleotide sequence of a DNA or RNA of a microorganism and of blocking, 30 for example, the expression of a polypeptide whose biological or structural activity is necessary for the growth or for the reproduction of the said microorganism.

Associated microorganism is understood to designate in the present invention any microorganism whose gene expression may be modulated, regulated, induced or inhibited, or whose growth or cellular replication may also be modulated by a compound of the invention. Associated microorganism is also understood to designate in the present invention any microorganism containing

15

20

nucleotide sequences or polypeptides according to the invention. These microorganisms may, in some cases, contain polypeptides or nucleotide sequences identical or homologous to those of the invention may also be detected and/or identified by the detection and/or identification methods or kit according to the invention and may also serve as a target for the compounds of the invention.

The invention relates to the compounds capable of being selected by a method of selection according to the invention.

The invention also relates to a pharmaceutical composition comprising a compound chosen from the following compounds:

a nucleotide sequence according to the invention;

a polypeptide or fusion polypeptide according to the invention;

a vector according to the invention;

an antibody according to the invention; and

a compound capable of being selected by a method of selection according to the invention, optionally in combination with a pharmaceutically acceptable vehicle or carrier.

An effective quantity is understood to designate a sufficient quantity of the said compound or antibody, or of a polypeptide of the invention, which makes it possible to modulate the growth of *Chlamydia trachomatis* or of an associated microorganism.

The invention also relates to a pharmaceutical composition according to the invention for the prevention or the treatment of an infection by a bacterium belonging to the species *Chlamydia trachomatis* or by an associated microorganism.

The invention relates, in addition, to an immunogenic and/or vaccine composition, characterized in that it comprises one or more polypeptides according to the invention and/or one or more hybrid polypeptides according to the invention.

The invention also comprises the use of a transformed cell according to the invention,
for the preparation of a vaccine composition.

The invention also relates to a vaccine composition, characterized in that it contains a nucleotide sequence according to the invention, a vector according to the invention and/or a transformed cell according to the invention.

The invention also relates to the vaccine compositions according to the invention, for the prevention or the treatment of an infection by a bacterium belonging to the species *Chlamydia trachomatis* or by an associated microorganism.

The invention also relates to the use of DNA encoding polypeptides of *Chlamydia trachomatis*, in particular antigenic determinants, to be formulated as vaccine compositions. In accordance with this aspect of the invention, the DNA of interest is engineered into an expression vector under the control of regulatory elements, which will promote expression of the DNA, *i.e.*,

WO 99/28475 PCT/IB98/01939

75

promoter or enhancer elements. In one preferred embodiment, the promoter element may be cell-specific and permit substantial transcription of the DNA only in predetermined cells. The DNA may be introduced directly into the host either as naked DNA (U.S. Patent No. 5,679,647 incorporated herein by reference in their entirety) or formulated in compositions with other agents which may facilitate uptake of the DNA including viral vectors, *i.e.*, adenovirus vectors, or agents which facilitate immunization, such as bupivicaine and other local anesthetics (U.S. Patent 5,593,972 incorporated herein by reference in their entirety), saponins (U.S. Patent 5,739,118 incorporated herein by reference in their entirety) and cationic polyamines (published international application WO 96/10038 incorporated herein by reference in their entirety).

The DNA sequence encoding the antigenic polypeptide and regulatory element may be inserted into a stable cell line or cloned microorganism, using techniques, such as targeted homologous recombination, which are well known to those of skill in the art, and described *e.g.*, in Chappel, U.S. Patent No. 4,215,051; Skoultchi, WO 91/06667 each of which is incorporated herein by reference in its entirety.

10

15

20

Such cell lines and microorganisms may be formulated for vaccine purposes. In yet another embodiment, the DNA sequence encoding the antigenic polypeptide and regulatory element may be delivered to a mammalian host and introduced into the host genome via homologous recombination (See, Chappel, U.S. Patent No. 4,215,051; Skoultchi, WO 91/06667 each of which is incorporated herein by reference in its entirety.

Preferably, the immunogenic and/or vaccine compositions according to the invention intended for the prevention and/or the treatment of an infection by *Chlamydia trachomatis* or by an associated microorganism will be chosen from the immunogenic and/or vaccine compositions comprising a polypeptide or one of its representative fragments corresponding to a protein, or one of its representative fragments, of the cellular envelope of *Chlamydia trachomatis*. The vaccine compositions comprising nucleotide sequences will also preferably comprise nucleotide sequences encoding a polypeptide or one of its fragments corresponding to a protein, or one of its representative fragments, of the cellular envelope of *Chlamydia trachomatis*.

Among these preferred immunogenic and/or vaccine compositions, the most preferred are those comprising a polypeptide or one of its representative fragments, or a nucleotide sequence or one of its representative fragments whose sequences are chosen from the nucleotide or amino acid sequences identified in this functional group and listed above.

The polypeptides of the invention or their representative fragments entering into the immunogenic compositions according to the invention may be selected by techniques known to persons skilled in the art, such as for example on the capacity of the said polypeptides to stimulate T cells, which results, for example, in their proliferation or the secretion of interleukins, and which

leads to the production of antibodies directed against the said polypeptides.

In mice, in which a weight dose of the vaccine composition comparable to the dose used in humans is administered, the antibody reaction is tested by collecting serum followed by a study of the formation of a complex between the antibodies present in the serum and the antigen of the vaccine composition, according to the customary techniques.

According to the invention, the said vaccine compositions will be preferably in combination with a pharmaceutically acceptable vehicle and, where appropriate, with one or more appropriate immunity adjuvants.

Various types of vaccines are currently available for protecting humans against infectious diseases: attenuated live microorganisms (M. bovis - BCG for tuberculosis), inactivated microorganisms (influenza virus), acellular extracts (Bordetella pertussis for whooping cough), recombinant proteins (hepatitis B virus surface antigen), polysaccharides (pneumococci). Experiments are underway on vaccines prepared from synthetic peptides or from genetically modified microorganisms expressing heterologous antigens. Even more recently, recombinant plasmid DNAs carrying genes encoding protective antigens were proposed as an alternative vaccine strategy. This type of vaccination is carried out with a particular plasmid derived from an E. coli plasmid which does not replicate in vivo and which encodes only the vaccinal protein. Animals were immunized by simply injecting the naked plasmid DNA into the muscle. This technique leads to the expression of the vaccine protein in situ and to a cell-type (CTL) and a humoral type (antibody) immune response.

20 This double induction of the immune response is one of the main advantages of the technique of vaccination with naked DNA.

The vaccine compositions of the present invention can be evaluated in *in vitro* and *in vivo* animal models prior to host, <u>e.g.</u>, human, administration. For example, *in vitro* neutralization assays such as those described by Peterson et al. (1988) can be utilized. The assay described by Peterson et al. (1988) is suitable for testing vaccine compositions directed toward either *Chlamydia trachomatis* or *Chlamydia pneumoniae*.

Briefly, hyper-immune antisera is diluted in PBS containing 5% guinea pig serum, as a complement source. Chlamydiae (10⁴ IFU; inclusion forming units) are added to the antisera dilutions. The antigen-antibody mixtures are incubated at 37°C for 45 minutes and inoculated into duplicate confluent Hep-2 or HeLa cell monolayers contained in glass vials (e.g., 15 by 45 mm), which have been washed twice with PBS prior to inoculation. The monolayer cells are infected by centrifugation at 1000X g for 1 hour followed by stationary incubation at 37° for 1 hour. Infected monolayers are incubated for 48 or 72 hours, fixed and stained with a Chlamydiae specific antibody, such as anti-MOMP for C. trachomatis, etc. Inclusion-bearing cells are counted in ten fields at a magnification of 200X. Neutralization titer is assigned based on the dilution that gives 50%

25

30

inhibition as compared to control monolayers/IFU.

The efficacy of vaccine compositions can be determined *in vivo* by challenging animal models of *Chlamydia trachomatis* infection, *e.g.*, guinea pigs or mice, with the vaccine compositions. For example, *in vivo* vaccine composition challenge studies in the guinea pig model of *Chlamydia trachomatis* infection can be performed. Briefly, female guinea pigs weighing 450 to 500 g are housed in an enviornmentally controlled room with a 12 hour light-dark cycle and immunized with vaccine compositions via a variety of immunization routes. Post-vaccination, guinea pigs are infected in the genital tract with the agent of guinea pig inclusion conjunctivitis (GPIC), which has been grown in HeLa or McCoy cells (Rank et al. (1988)). Each animal receives approximately 1.4x10⁷ inclusion forming units (IFU) contained in 0.05 ml of sucrose-phosphate-glutamate buffer, pH 7.4 (Schacter, J. (1980)). The course of infection monitored by determining the percentage of inclusion-bearing cells by indirect immunofluorescence with GPIC specific antisera, or by Giemsastained smear from a scraping from the genital tract (Rank et al. (1988)). Antibody titers in the serum is determined by an enzyme-linked immunosorbent assay.

Alternatively, in vivo vaccine composition challenge studies can be performed in the murine model of *Chlamydia trachomatis* (Morrison et al., 1995). Briefly, female mice 7 to 12 weeks of age receive 2.5 mg of depoprovera subcutaneously at 10 and 3 days before vaginal infection. Post-vaccination, mice are infected in the genital tract with 1,500 inclusion-forming units of *Chlamydia trachomatis* contained in 5ml of sucrose-phosphate-glutamate buffer, pH. 7.4. The course of infection is monitored by determining the percentage of inclusion-bearing cells by indirect immunofluorence with *Chlamydia trachomatis* specific antisera, or by a Giemsa-stained smear from a scraping from the genital tract of an infected mouse. The presence of antibody titers in the serum of a mouse is determined by an enzyme-linked immunosorbent assay.

The vaccine compositions comprising nucleotide sequences or vectors into which the said sequences are inserted are in particular described in International Application No. WO 90/11092 and also in International Application No. WO 95/11307.

The nucleotide sequence constituting the vaccine composition according to the invention may be injected into the host after having been coupled to compounds which promote the penetration of this polynucleotide inside the cell or its transport up to the cell nucleus. The resulting conjugates may be encapsulated into polymeric microparticles, as described in International Application No. WO 94/27238 (Medisorb Technologies International).

According to another embodiment of the vaccine composition according to the invention, the nucleotide sequence, preferably a DNA, is complexed with the DEAE-dextran (Pagano et al., 1967) or with nuclear proteins (Kaneda et al., 1989), with lipids (Felgner et al., 1987) or encapsulated into liposomes (Fraley et al., 1980) or alternatively introduced in the form of a gel

facilitating its transfection into the cells (Midoux et al., 1993, Pastore et al., 1994). The polynucleotide or the vector according to the invention may also be in suspension in a buffer solution or may be combined with liposomes.

Advantageously, such a vaccine will be prepared in accordance with the technique described by Tacson et al. or Huygen et al. in 1996 or alternatively in accordance with the technique described by Davis et al. in International Application No. WO 95/11307.

Such a vaccine may also be prepared in the form of a composition containing a vector according to the invention, placed under the control of regulatory elements allowing its expression in humans or animals. It is possible, for example, to use, as vector for the *in vivo* expression of the polypeptide antigen of interest, the plasmid pcDNA3 or the plasmid pcDNA1/neo, both marketed by Invitrogen (R & D Systems, Abingdon, United Kingdom). It is also possible to use the plasmid V1Jns.tPA, described by Shiver et al. in 1995. Such a vaccine will advantageously comprise, in addition to the recombinant vector, a saline solution, for example a sodium chloride solution.

The immunogenic compositions of the invention can be utilized as part of methods of immunization, wherein such methods comprise administering to a host, e.g., a human host, an immunizing amount of the immunogenic compositions of the invention. In a preferred embodiment, the method of immunizing is a method of immunizing against *Chlamydia trachomatis*.

A pharmaceutically acceptable vehicle is understood to designate a compound or a combination of compounds entering into a pharmaceutical or vaccine composition which does not cause side effects and which makes it possible, for example, to facilitate the administration of the active compound, to increase its life and/or its efficacy in the body, to increase its solubility in solution or alternatively to enhance its preservation. These pharmaceutically acceptable vehicles are well known and will be adapted by persons skilled in the art according to the nature and the mode of administration of the active compound chosen.

As regards the vaccine formulations, these may comprise appropriate immunity adjuvants which are known to persons skilled in the art, such as, for example, aluminium hydroxide, a representative of the family of muramyl peptides such as one of the peptide derivatives of N-acetyl-muramyl, a bacterial lysate, or alternatively incomplete Freund's adjuvant, StimulonTM QS-21 (Aquila Biopharmaceuticals, Inc., Framinham, MA), MPLTM (3-0-deacylated monophosphoryl lipid A; RIBI ImmunoChem Research, Inc., Hamilton, MT), aluminum phosphate, IL-12 (Genetics Institute, Cambridge, MA).

25

35

Preferably, these compounds will be administered by the systemic route, in particular by the intravenous route, by the intranasal, intramuscular, intradermal or subcutaneous route, or by the oral route. More preferably, the vaccine composition comprising polypeptides according to the invention will be administered several times, spread out over time, by the intradermal or subcutaneous

route.

Their optimum modes of administration, dosages and galenic forms may be determined according to criteria which are generally taken into account in establishing a treatment adapted to a patient, such as for example the patient's age or body weight, the seriousness of his general condition, tolerance of the treatment and the side effects observed.

The invention comprises the use of a composition according to the invention for the treatment or the prevention of genital diseases which are induced or worsened by *Chlamydia trachomatis*.

Finally, the invention comprises the use of a composition according to the invention for the treatment or the prevention of eye diseases which are induced or worsened by the presence of *Chlamydia trachomatis*.

Finally, the invention comprises the use of a composition according to the invention for the treatment or the prevention of systemic diseases, especially of the lymphatic system, which are induced or worsened by the presence of *Chlamydia trachomatis*.

Other characteristics and advantages of the invention appear in the following examples and figures:

Legend to the figures:

Figure 1: Line for the production of Chlamydia trachomatis sequences

20 Figure 2: Analysis of the sequences and assembling

Figure 3: Finishing techniques

Figure 3a): Assembly map

Figure 3b): Determination and use of the orphan ends of the contigs

25 EXAMPLES

Cells

The Chlamydia trachomatis LGV2 strain used is identified to have over 98% homology with the outer membrane protein sequences omp1 (CHTMOMPA) and omp2 (CHTOMP2A) of the Chlamydia trachomatis serovar L2/434/Bu strain.

The Chlamydia trachomatis LGV2 strain is cultured on mouse fibroblasts (McCoy cells), obtained from the American Type Culture Collection, under the reference ATCC CRL-1696.

Culture of the cells

The mouse fibroblasts are cultured in 75-ml cell culture flasks (Corning). The culture medium is Dulbecco's modified cell culture medium (Gibco BRL No. 04101965) supplemented with

MEM amino acids (Gibco BRL - No. 04301140) L (5 ml per 500 ml of medium) and 5% foetal calf serum (Gibco BRL No. 10270 batch 40G8260K) without antibiotics or antifungals.

The cell culture stock is maintained in the following manner. The cell cultures are examined under an inverted microscope. 24 hours after confluence, each cellular lawn is washed with PBS (Gibco BRL No. 04114190), rinsed and then placed for 5 min in an oven in the presence of 3 ml of trypsine (Gibco BRL No. 25200056). The cellular lawn is then detached and then resuspended in 120 ml of culture medium, the whole is stirred in order to make the cellular suspension homogeneous. 30 ml of this suspension are then distributed per cell culture flask. The flasks are kept in a CO₂ oven (5%) for 48 hours at a temperature of 37°C. The cell stock is maintained so as to have available daily 16 flasks of subconfluent cells. It is these subconfluent cells which will be used so as to be infected with Chlamydia. 25-ml cell culture flasks are also used, these flasks are prepared in a similar manner but the volumes used for maintaining the cells are the following: 1 ml of trypsine, 28 ml of culture medium to resuspend the cells, 7 ml of culture medium are used per 25-ml flask.

Infection of the cells with Chlamydia

Initially, the Chlamydiae are obtained frozen (at -70°C), in suspension in a volume of 1 millilitre. This preparation is slowly thawed, 500 µl are collected and brought into contact with subconfluent cells, which are obtained as indicated above, in a 25-ml cell culture flask, containing 1 ml of medium, so as to cover the cells. The flask is then centrifuged at 2000 rpm in a «swing» rotor for microtitre plates, the centrifuge being maintained at a temperature of 35°C. After centrifugation, the two flasks are placed in an oven at 35°C for three hours. 6 ml of culture medium containing cycloheximide (1 µg/ml) are then added and the flask is stored at 35°C. After 48 hours, the level of infection is evaluated by direct immunofluorescence and by the cytopathogenic effect caused to the cells.

25

15

Direct immunofluorescence

Starting with infected cells, which were obtained as indicated above, a cellular smear is deposited with a Pasteur pipette on a microscope slide. The cellular smear is fixed with acetone for 10 minutes; after draining the acetone, the smear is covered with 30 µl of murine monoclonal antibodies directed against MOMP (major outer membrane protein) of Chlamydia (Syva, Biomérieux) labelled with fluorescein isothiocyanate. The whole is then incubated in a humid chamber at a temperature of 37°C. The slides are then rinsed with water, slightly dried, and then after depositing a drop of mounting medium, a coverslip is mounted before reading. The reading is carried out with the aid of a fluorescence microscope equipped with the required filters (excitation at 490 nm, emission at 520 nm).

25

Harvesting of the Chlamydia trachomatis

After checking the infection by direct immunofluorescence, carried out as indicated above, the culture flasks are opened under a sterile cabinet, sterile glass beads with a diameter of the order of a millimeter are placed in the flask. The flask is closed and then vigorously stirred while being maintained horizontally, the cellular lawn at the bottom, so that the glass beads can have a mechanical action on the cellular lawn. Most of the cells are thus detached or broken; the effect of the stirring is observed under an optical microscope so as to ensure proper release of Chlamydiae.

Large-scale infection of the cell cultures

The product of the Chlamydiae harvest (culture medium and cellular debris) is collected with a pipette, and distributed into three cell culture flasks containing subconfluent L cells, obtained as indicated above. The cells thus inoculated are placed under gentle stirring (swing) in an oven at 35°C. After one hour, the flasks are kept horizontally in an oven so that the culture medium covers the cells for 3 hours. 30 ml of culture medium containing actydione (1 µg/ml) are then added to each of the flasks. The culture flasks are then stored at 35°C for 48 hours. The cells thus infected are examined under an optical microscope after 24 hours, the cytopathogenic effect is evaluated by the appearance of cytoplasmic inclusions which are visible under an inverted optical microscope. After 48 hours, the vacuoles containing the Chlamydiae occupy the cytoplasm of the cell and push the cell nucleus sideways. At this stage, numerous cells are spontaneously destroyed and have left free elementary bodies in the culture medium. The Chlamydiae are harvested as described above and are either frozen at -80°C or used for another propagation.

Purification of the Chlamydiae

The product of the Chlamydia harvests, stored at -80°C, is thawed on a water bath at room temperature. After thawing, each tube is vigorously stirred for one minute and immersed for one minute in an ultrasound tank (BRANSON 1200); the tubes are then stirred by inverting before being centrifuged for 5 min at 2000 rpm. The supernatant is carefully removed and kept at cold temperature (ice). The supernatant is vigorously stirred and then filtered on nylon filters having pores of 5 microns in diameter on a support (Nalgene) allowing a delicate vacuum to be established under the nylon filter. For each filtration, three nylon filters are superposed; these filters are replaced after every 40 ml of filtrate. Two hundred milliliters of filtration product are kept at cold temperature, and then after stirring by inverting, are centrifuged at 10,000 rpm for 90 min, the supernatant is removed and the pellet is taken up in 10 ml of 10 mM Tris, vigorously vortexed and then centrifuged at 10,000 rpm for 90 min. The supernatant is removed and the pellet is taken up in a buffer (20 mM Tris pH 8.0, 50 mM

KCl, 5 mM MgCl₂) to which 800 units of DNAse I (Boehringer) are added. The whole is kept at 37°C for one hour. One ml of 0.5 M EDTA is then added, and the whole is vortexed and frozen at -20°C.

Preparation of the DNA

5

25

The Chlamydiae purified above are thawed and subjected to a proteinase K (Boehringer) digestion in a final volume of 10 ml. The digestion conditions are the following: 0.1 mg/ml proteinase K, 0.1 % SDS at 55°C, stirring every 10 min. The product of digestion is then subjected to a double extraction with phenol-chloroform, two volumes of ethanol are added and the DNA is directly recovered with a Pasteur pipette having one end in the form of a hook. The DNA is 10 dried on the edge of the tube and then resuspended in 500 µl of 2 mM Tris pH 7.5. The DNA is stored at 4°C for at least 24 hours before being used for the cloning.

Cloning of the DNA

After precipitation, the DNA is quantified by measuring the optical density at 260 nm. Thirty µg of Chlamydia DNA are distributed into 10 tubes of 1.5 ml and diluted in 300 µl of water. Each of the tubes is subjected to 10 applications of ultrasound lasting for 0.5 sec in a sonicator (Unisonix XL2020). The contents of the 10 tubes are then grouped and concentrated by successive extractions with butanol (Sigma B1888) in the following manner: two volumes of butanol are added to the dilute DNA mixture. After stirring, the whole is centrifuged for five minutes at 2500 rpm and 20 the butanol is removed. This operation is repeated until the volume of the aqueous phase is less than 1 ml. The DNA is then precipitated in the presence of ethanol and of 0.5 M sodium acetate pH 5.4, and then centrifuged for thirty minutes at 15,000 rpm at cold temperature (4°C). The pellet is washed with 75% ethanol, centrifuged for five minutes at 15,000 rpm and dried at room temperature. A tenth of the preparation is analysed on a 0.8% agarose gel. Typically, the size of the DNA fragments thus prepared is between 200 and 8000 base pairs.

To allow the cloning of the DNA obtained, the ends are repaired. The DNA is distributed in an amount of 10 µg/tube, in the following reaction medium: 100 µl final volume, 1 H buffer (Biolabs 201L), 0.5 µl BSA 0.05 mg/ml, 0.1 mM dATP, 0.1 mM each of dGTP, dCTP or dTTP, 60,000 IU T4 DNA polymerase. The reaction is incubated for thirty minutes at 16°C. The 30 contents of each of the tubes are then grouped before carrying out an extraction with phenolchloroform and then precipitating the aqueous phase as described above. After this step, the DNA thus prepared is phosphorylated. For that, the DNA is distributed into tubes in an amount of 10 µg per tube, and then in a final volume of 50 µl, the reaction is prepared in the following manner: 1 mM ATP, 1 x kinase buffer, 10 IU T4 polynucleotide kinase (Biolabs 201L). The preparation is incubated 35 for thirty minutes at 37°C. The contents of the tubes are combined and a phenol-chloroform extraction WO 99/28475 PCT/IB98/01939

83

and then a precipitation are carried out in order to precipitate the DNA. The latter is then suspended in 1 µl of water and then the DNA fragments are separated according to their size on a 0.8% agarose gel (1 x TAE). The DNA is subjected to an electric field of 5 V/cm and then visualized on a UV table. The fragments whose size varies between 1200 and 2000 base pairs are selected by cutting out the gel. The gel fragment thus isolated is placed in a tube and then the DNA is purified with the Qiaex kit (20021 Qiagen), according to the procedure provided by the manufacturer.

Preparation of the vector

15

20

25

35

14 µg of the cloning vector pGEM-5Zf (Proméga P2241) are diluted in a final volume 10 of 150 µl and are subjected to digestion with the restriction enzyme EcoRV 300 IU (Biolabs 195S) according to the protocol and with the reagents provided by the manufacturer. The whole is placed at 37°C for 150 min and then distributed in the wells of a 0.8% agarose gel subjected to an electric field of 5 V/cm. The linearized vector is visualized on a UV table, isolated by cutting out the gel and then purified by the Qiaex kit (Qiagen 20021) according to the manufacturer's recommendations. The purification products are grouped in a tube, the volume is measured and then half the volume of phenol is added and the whole is vigorously stirred for 1 min. Half the volume of chloroform-isoamyl alcohol 24:1 is added and vigorously stirred for 1 min. The whole is centrifuged at 15,000 rpm for 5 min at 4°C, the aqueous phase is recovered and transferred into a tube. The DNA is precipitated in the presence of 0.3 M sodium acetate, pH 5.4 and 3 volumes of ethanol and placed at -20°C for 1 hour. The DNA is then centrifuged at 15,000 rpm for 30 min at 4°C, the supernatant is removed while preserving the pellet, washed twice with 70% ethanol. After drying at room temperature, the DNA is suspended in 25 µl of water.

Phosphorylation of the vector

25 µl of the vector prepared in the preceding step are diluted in a final volume of 500 µl of the following reaction mixture:

After repair, the DNA is subjected to a phenol-chloroform extraction and a precipitation, the pellet is then taken up in 10 µl of water, the DNA is quantified by measuring the optical density at 260 nm. The quantified DNA is ligated into the vector PGEm-5Zf(+) prepared by the restriction enzyme EcoRV and dephosphorylated (see preparation of the vector). The ligation is carried out under three conditions which vary in the ratio between the number of vector molecules and the number of insert molecules. Typically, an equimolar ratio, a ratio of 1:3 and a ratio of 3:1 are used for the ligations which are, moreover, carried out under the following conditions: vector PGEm-5Zf(+) 25 ng, cut DNA, ligation buffer in a final volume of 20 µl with T4 DNA ligase (Amersham E70042X); the whole is then placed in a refrigerator overnight and then a phenol-

20

chloroform extraction and a precipitation are carried out in a conventional manner. The pellet is taken up in 5 μ l of water.

Transformation of the bacteria

Plating of the bacteria

Petri dishes containing LB Agar medium containing ampicillin (50 μg/ml), Xgal (280 μg/ml) [5-bromo-4-chloro-indolyl-beta-D-galactopyranoside (Sigma B-4252)], IPTG (140 μg/ml) [isopropyl-beta-D-thiogalactoside (Sigma I-6758)] are used, 50 and 100 μl of bacteria are plated for each of the ligations. The Petri dishes are placed upside down at 37°C for 15 to 16 hours in an oven.

The number of «recombinant» positive clones is evaluated by counting the white colonies and the blue colonies which are thought to contain the vector alone.

Evaluation of the «recombinant» positive clones:

Ninety-four white colonies and two blue colonies are collected with the aid of sterile cones and are deposited at the bottom of the wells of plates designed for carrying out the amplification techniques. 30 µl of the following reaction mixture are added to each well: 1.7 mM MgCl₂, 0.2 mM each of dATP, dCTP, dGTP and dTTP, two synthetic oligonucleotides corresponding to sequences flanking the cloning site on either side and orienting the synthesis of the DNA in a convergent manner (0.5 µM RP and PU primers, 1 U TAQ polymerase (GibcoBRL 18038-026)).

The colonies thus prepared are subjected to a temperature of 94°C for 5 min and then to 30 thermal cycles composed of the following steps: 94°C for 40 s, 50°C for 30 s, 72°C for 180 s. The reaction is then kept for 7 min at 72°C and then kept at 4°C.

The amplification products are deposited on an agarose gel (0.8%), stained with ethidium bromide, subjected to electrophoresis, and then analysed on an ultraviolet table. The presence of an amplification fragment having a size greater than 500 base pairs indicates the presence of an insert. The bacterial clones are then prepared so as to study the sequence of their insert.

Sequencing

To sequence the inserts of the clones obtained as above, these were amplified by PCR on bacteria cultures carried out overnight using the primers for the vectors flanking the inserts. The sequence of the ends of these inserts (on average 500 bases on each side) was determined by automated fluorescent sequencing on an ABI 377 sequencer, equipped with the ABI Prism DNA Sequencing Analysis software (version 2.1.2).

15

20

25

The sequences obtained by sequencing in a high-yield line (Figure 1) are stored in a database; this part of the production is independent of any treatment of the sequences. The sequences are extracted from the database, avoiding all the regions of inadequate quality, that is to say the regions for which uncertainties are observed on the sequence at more than 95%. After extraction, the sequences are introduced into a processing line, the diagram of which is described in Figure 2. In a first path of this processing line, the sequences are assembled by the Gap4 software from R. Staden (Bonfield et al., 1995) (OS UNIX/SUN Solaris); the results obtained by this software are kept in the form of two files which will be used for a subsequent processing. The first of these files provides information on the sequence of each of the contigs obtained. The second file represents all the clones participating in the composition of all the contigs as well as their positions on the respective contigs.

The second processing path uses a sequence assembler (TIGR-Asmg assembler UNIX/SUN Solaris); the results of this second processing path are kept in the form of a file in the TIGR-Asmg format which provides information on the relationship existing between the sequences selected for the assembly. This assembler is sometimes incapable of linking contigs whose ends overlap over several hundreds of base pairs.

The results obtained from these two assemblers are compared with the aid of the BLAST program, each of the contigs derived from one assembly path being compared with the contigs derived from the other path.

For the two processing paths, the strict assembly parameters are fixed (95% homology, 30 superposition nucleotides). These parameters avoid 3 to 5% of the clones derived from eukaryotic cells being confused with sequences obtained from the clones derived from *Chlamydia trachomatis*. The eukaryotic sequences are however preserved during the course of this project; the strategy introduced, which is described below, will be designed, inter alia, not to be impeded by these sequences derived from contaminating clones.

The results of these two assemblers are processed in a software developed for this project. This software operates on a Windows NT platform and receives, as data, the results derived from the STADEN software and/or the results derived from the TIGR-Asmg assembler, the software, results, after processing of the data, in the determination of an assembly map which gives the proximity relationship and the orientation of the contigs in relation to one another (Figure 3a). Using this assembly map, the software determines all the primers necessary for finishing the project. This treatment, which will be detailed below, has the advantage of distinguishing the isolated sequences derived from the contaminations, by the DNA eukaryotic cells, of the small-sized sequences clearly integrated into the project by the relationships which they establish with contigs. In order to allow, without any risk of error, the arrangement and the orientation of the contigs in relation to one another, a statistical evaluation of the accuracy of the names «naming» of sequence is made from the results of

«contigation». This evaluation makes it possible to give each of the clone plates, as well as each of the subsets of plates, a weight which is inversely proportional to probable error rate existing in the «naming» of the sequences obtained from this plate or from a subset of this plate. In spite of a low error rate, errors may occur throughout the steps of production of the clones and of the sequences. 5 These steps are numerous, repetitive and although most of them are automated, others, like the deposition in the sequencers, are manual; it is then possible for the operator to make mistakes such as the inversion of two sequences. This type of error has a repercussion on the subsequent processing of the data, by resulting in relationships (between the contigs) which do not exist in reality, then in attempts at directed sequencing between the contigs which will end in failure. It is because of this that 10 the evaluation of the naming errors is of particular importance since it allows the establishment of a probabilistic assembly map from which it becomes possible to determine all the clones which will serve as template to obtain sequences separating two adjacent contigs. Table 2 of parent U.S. Application Serial No. 60/107077 filed November 4, 1998, French application 97-15041 filed November 28, 1997 and French application 97-16034 filed December 17, 1997, each of which is incorporated by reference herein in its entirety, gives the clones and the sequences of the primers initially used during the initial operations.

To avoid the step which consists in ordering and then preparing the clones by conventional microbiological means, outer and inner primers oriented towards the regions not yet sequenced are defined by the software. The primers thus determined make it possible to prepare, by 20 PCR, a template covering the nonsequenced region. It is the so-called outer primers (the ones most distant from the region to be sequenced) which are used to prepare this template. The template is then purified and a sequence is obtained on each of the two strands during 2 sequencing reactions which each use one of the 2 inner primers. In order to facilitate the use of this approach, the two outer primers and the two inner primers are prepared and then stored on the same position of 4 different 25 96-well plates. The two plates containing the outer primers are used to perform the PCRs which serve to prepare the templates. These templates will be purified on purification columns preserving the topography of the plates. Each of the sequences are obtained using primers situated on one and then on the other of the plates containing the inner primers. This distribution allows a very extensive automation of the process and results in a method which is simple to use for finishing the regions not yet sequenced. Table 3 of parent U.S. Application Serial No. 60/107077 filed November 4, 1998, French application 97-15041 filed November 28, 1997 and French application 97-16034 filed December 17, 1997, each of which is incorporated by reference herein in its entirety, gives the names and the sequences of the primers used for finishing Chlamydia trachomatis.

Finally, a number of contigs exist in a configuration where one of their ends is not linked to any other contig end (Figure 3b) by a connecting clone relationship (a connecting clone is

defined as a clone having one sequence end on a contig and the other end of its sequence on another contig; furthermore, this clone must be derived from a plate or a subset of plates with adequate naming quality). For the *Chlamydia trachomatis* project, this particular case occurred 37 times. Two adjacent PCR primers orienting the synthesis of the DNA towards the end of the consensus sequence are defined for each of the orphan ends of the consensus sequence. The primer which is closest to the end of the sequence is called the inner primer whereas the primer which is more distant from the end of the sequence is called the outer primer. The outer primers are used to explore the mutual relationship between the orphan ends of the different contigs. The presence of a single PCR product and the possibility of amplifying this product unambiguously using the inner primers evokes the probable relationship between the contigs on which the primers which allowed the amplification are situated. This relationship will be confirmed by sequencing and will allow the connection between the orphan ends of the consensus sequences. This strategy has made it possible to obtain a complete map of the *Chlamydia trachomatis* chromosome and then to finish the project.

15 Quality control

30

All the bases not determined with certainty in the chromosomal sequence were noted and the density of uncertainties was measured on the entire chromosome. The regions with a high density of uncertainties were noted and the PCR primers spanning these regions were drawn and are represented in Table 4 of parent U.S. Application Serial No. 60/107077 filed November 4, 1998, French application 97-15041 filed November 28, 1997 and French application 97-16034 filed December 17, 1997 each of which is incorporated by reference herein in its entirety.

Data banks

Local reorganizations of major public banks were used. The protein bank used consists of the nonredundant fusion of the Genpept bank (automated translation of GenBank, NCBI; Benson et al., 1996).

The entire BLAST software (public domain, Altschul et al., 1990) for searching for homologies between a sequence and protein or nucleic data banks was used. The significance levels used depend on the length and the complexity of the region tested as well as the size of the reference bank. They were adjusted and adapted to each analysis.

The results of the search for homologies between a sequence according to the invention and protein or nucleic data banks are presented and summarized in Table 1 below.

Table 1: <u>List of coding chromosome regions and homologies between these regions and the sequence</u>

35 <u>banks.</u>

Legend to Table 1: Open reading frames are identified with the GenMark software version 2.3A (GenePro), the template used is *Chlamydia trachomatis* of order 4 on a length of 196 nucleotides with a window of 12 nucleotides and a minimum signal of 0.5. These reading frames are numbered in order of appearance on the chromosome, starting with ORF2 (ORF column). The positions of the beginning and of the end are then given in column 2 (position). When the position of the beginning is greater than the position of the end, this means that the region is encoded by the strand complementary to the sequence which was given in the sequence SEQ ID No. 1.

All the putative products were subjected to a search for homology on GENPEPT (release 103 for SEQ ID No. 2 to SEQ ID No. 1076 and release 108 for SEQ ID No. 1077 to SEQ ID No. 1197 with the BLASTp software (Altschul et al. 1990), with, as parameters, the default parameters with the exception of the expected value E set at 10⁻⁵ (for SEQ ID No. 2 to SEQ ID No. 1076) and P value set at e⁻¹⁰ (for SEQ ID No. 1077 to SEQ ID No. 1197). Subsequently, only the identities greater than 30% (I% column) were taken into account. The description of the most homologous sequence is given in the Homology column; the identifier for the latter sequence is given in the ID column and the animal species to which this sequence belongs is given in the Species column. The Homology score is evaluated by the sum of the blast scores for each region of homology and reported in the Score column. Table 1 also reflects data from additional ORF finder programs as defined below.

Materials and methods: transmembrane domains:

The DAS software was used as recommended by the authors (Cserzo et al., 1997).

This method uses, to predict the transmembrane domains, templates derived from a sampling of selected proteins. All the regions for which a "Cutoff" greater than 1.5 was found by the program were taken into account.

25

20

Additional ORF Finder Programs

For this analysis, two additional ORF finder programs were used to predict potential open reading frames of a minimum length of 74 amino acids; Glimmer (Salzberg, S.L., Delcher, A., Kasif, S., and W. White. 1998. Microbial gene identification using interpolated Markov models.

Nucleic Acids Res. 26:544-548.), and an in-house written program. The in-house program used a very simple search algorithm. The analysis required the that the genomic DNA sequence text be in the 5' to 3' direction, the genome is circular, and that TAA, TAG, and TGA are stop codons. The search parameters were as follows:

(1) A search for an ORF that started with a GTG codon was performed. If no GTG codons were found, then a search for an ATG codon was performed. However, if a GTG codon was found,

then a search downstream for a ATG codon was performed. All start and stop nucleotide positions were recorded.

- (2) A search for an ORF that started with a TTG codon was performed. If no TTG codons were found, then a search for a ATG codon was performed. However, if a TTG codon was found, then a search downstream for a ATG codon was performed. All start and stop nucleotide positions were recorded.
- (3) The analysis described in steps 1 and 2 were repeated for the opposite strand of DNA sequence.
- (4) A search for ORFs that determined all ORF lengths using start and stop positions in the same reading frames was performed.
 - (5) All ORFs whose DNA length was less than 225 nucleotides were eliminated from the search.

Surface Exposed Protein Search Criteria

Potential cell surface vaccine targets are outer membrane proteins such as porins, lipoproteins, adhesions and other non-integral proteins. In *Chlamydia psittaci*, the major immunogens is a group of putative outer membrane proteins (POMPs) and no homologs have been found in *Chlamydia trachomatis* and *Chlamydia trachomatis* by traditional analysis (Longbottom, D., Russell, M., Dunbar, S.M., Jones, G.E., and A.J. Herring. 1998. Molecular Cloning and Characterization of the Genes Coding for the Highly Immunogenic Cluster of 90-Kilodalton Envelope Proteins from *Chlamydia psittaci* Subtype That Causes Abortion in Sheep. Infect Immun 66:1317-1324.) However, utilizing the criteria described below, several ORFs encoding outer membrane proteins have been identified in *Chlamydia trachomatis*, all of which may represent vaccine candidates. Any ORF which met any one of the criteria described below were considered to encode a surface exposed protein.

Protein homology searches of the translated ORFs were done using the Blastp 2.0 tool (Altschul, S.F., Madden, T.L., Schaffer, A.A., Zhang, J., Zhang, Z., Miller, W., and D.J. Lipman. 1997. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402). An ORF was labeled surface exposed if the translated ORF had homology to a known, or hypothetical, or putative surface exposed protein with a P score less than e^{-10} .

Most, if not all, proteins that are localized to the membrane of bacteria, via a secretory pathway, contain a signal peptide. The software program SignalP, was used to analyze the amino acid sequence of an ORF for such a signal peptide (Nielsen, H., Engelbrecht. J., Brunak, S., and G. von Heijne. 1997. Identification of prokaryotic and eukaryotic signal peptides and prediction

of their cleavage sites. Protein Engineering 10:1-6.) The first 60 N-terminal amino acids of each ORF were analyzed by SignalP using the Gram-negative software database. The output generates four separate values, maximum C, maximum Y, maximum S, and mean S. The S-score, or signal region, is the probability of the position belonging to the signal peptide. The C-score, or cleavage site, is the probability of the position being the first in the mature protein. The Y-score is the geometric average of the C-score and a smoothed derivative of the S-score. A conclusion of either a Yes or No is given next to each score. If all four conclusions are Yes and the C-terminal amino acid is either a phenylalanine (F) or a tyrosine (Y), the ORF was labelled outer membrane (Struyve, M., Moons, M., and J. Tommassen. 1991. Carboxy-terminal Phenylalanine is Essential for the Correct Assembly of a Bacterial Outer Membrane Protein. J. Mol. Biol. 218:141-148.)

The program called Psort was used to determine the localization of a protein based on its signal sequence, recognition of transmembrane segments, and analysis of its amino acid composition (Nakai, K., and M. Kanehisa. 1991. Expert system for predicting protein localization sites in gram-negative bacteria. Proteins 11:95-110.) An ORF is considered to be an outer membrane protein if the output data predicts the ORF encoded protein as outer membrane with a certainty value of 0.5 or better and whose value is at least twice as large as the next predicted localized certainty value.

Finally, ORFs that were not predicted to be outer membrane or surface exposed, based on the above criteria, were further analyzed. The Blastp output data for these ORFs were searched using various general and specific keywords, suggestive of known cell surface exposed proteins. An ORF was labeled surface exposed if the keywords matched had a Blastp hit with a P score less than e⁻¹⁰, and there was no better data indicating otherwise. The following is a list of the searched keywords:

25	Adhesion	Adhesin	Invasin
	Invasion	Extension	Omp
	Outer Surface	Porin	Outer Membrane
	Cell Surface	Cell Wall	Pilin
	Flagellar sheath	Cir	ChuA
30	СорВ	ExeD	FadL
	FecA	FepA	FhuA
	FmdC	FomA	FrpB
	GspD	HemR	HgbA
	Ндр	HmbR	HmuR
35	HMW	HrcC	Hrp

WO 99/28475 PCT/IB98/01939

91

	InvG	LamB	LbpA
	LcrQ	Lmp1	MxiD
	MOMP	PilE	HpaA
	NolW	NspA	OpcP
5	OpnP	Opr	OspA
	PhoE	PldA	Por
	PscC	PulD	PupA
	QuiX	RafY	ScrY
	SepC	ShuA	SomA
10	SpiA	Tbp1	Yop
	YscC	mip	Tol
	Pilus	BtuB	

20

Those ORFs that did not meet the minimum requirement for being an outer membrane protein based on the above search criteria but which were homologous to identified outer membrane ORFs in 15 Chlamydia pneumoniae were included. The Chlamydia pneumoniae genome (French patent application No. 97-14673, filed 21 November 1997) was analyzed using the above search criteria and a number of outer membrane ORFs were identified. These Chlamydia pneumoniae ORFs were then tested against the Chlamydia trachomatis genome using Blastp. Any Chlamydia trachomatis ORF with a Blastp P value less than e-10 against a Chlamydia pneumoniae outer membrane was included in this section, if there was no better data indicating otherwise. A list of ORFs in the Chlamydia trachomatis genome encoding putative surface exposed proteins is set forth above in the specification.

Identification of Putative Lipoproteins in the Genome of Chlamydia trachomatis

Lipoproteins are the most abundant post-translationally modified bacterial secretory proteins (Pugsley, A. P.. 1993. The complete general secretory pathway in Gram-negative bacteria. Microbiol. Rev. 57:50-108). The characteristic features of lipoproteins are a thiol-linked diacylglyceride and an amine-linked monoacyl group on the cysteine that becomes the amino-terminal residue after signal peptide cleavage by Signal Peptidase II. (Pugsley, A. P., 1993. The complete general secretory pathway in Gram-negative bacteria. Microbiol. Rev. 57:50-108). The identification of putative lipoproteins from the genomic sequencing of Chlamydia trachomatis was done by examining the deduced amino acid sequence of identified ORFs for the presence of a signal peptide with a Signal Peptidase II cleavage site analogous to the consensus sequence for prolipoprotein modification and processing reactions (Hayashi, S., and H. C. Wu. 1992. Identification and characterization of lipid-modified proteins in bacteria, p. 261-285. In N. M. Hooper and A. J. Turner (ed.) Lipid modification of proteins: A practical approach. Oxford University Press, New York; Sutcliffe, I. C. and R. R. B. Russell. 1995. Lipoproteins of Gram-positive bacteria. J. Bacteriol. 177:1123-1128).

The deduced amino acid sequences of Chlamydia trachomatis ORFs were initially screened for the most basic of lipoprotein characteristics, a cysteine in the first 30 amino acids of the deduced protein. ORFs with a standard start codon (ATG, GTG, or TTG) and having one or more of the following characteristics were selected for direct analysis of their first 30 amino acids:

- Significant Signal P value (at least two out-of-the four values are Yes)
- PSORT value indicating membrane passage (IM-inner membrane, Peri-periplasm, or (b) OM-outer membrane)
 - (c) Identification of the word lipoprotein among the ORF Blastp data set.

10

15

25

30

A Blastp value of <e.10 with a putative lipoprotein from Chlamydia pneumoniae (d) (French application No. 97-14673 filed 21 November 1997).

The first 30 amino acids encoded by each ORF in this set were analyzed for the characteristics commonly found in lipoprotein signal peptides (Pugsley, A. P., 1993. The complete general secretory pathway in Gram-negative bacteria. Microbiol. Rev. 57:50-108; Hayashi, S., and H. C. Wu. 1992. Identification and characterization of lipid-modified proteins in bacteria, p. 261-285. In N. M. Hooper and A. J. Turner (ed.) Lipid modification of proteins: A practical approach. Oxford University Press, New York; Sutcliffe, I. C. and R. R. B. Russell. 1995. Lipoproteins of Grampositive bacteria. J. Bacteriol. 177:1123-1128.) Putative lipoprotein signal peptides were required to have a cysteine between amino acid 10 and 30 and reach a minimum score of three based on the following criteria for lipoprotein signal peptides:

- (a) Identification of specific amino acids in specific positions around the cysteine which are part of the consensus Signal Peptidase II cleavage site (Hayashi, S., and H. C. Wu. 1992. Identification and characterization of lipid-modified proteins in bacteria, p. 261-285. In N. M. Hooper and A. J. Turner (ed.) Lipid modification of proteins: A practical approach. Oxford University Press, New York); Sutcliffe, I. C. and R. R. B. Russell. 1995. Lipoproteins of Gram-positive bacteria. J. Bacteriol. 177:1123-1128). identification of the cleavage site is the most important factor in identifying putative lipoproteins, each correctly positioned amino acid contributed toward reaching the minimum score of three.
- (b) A hydrophobic region rich in alanine and leucine prior to the cleavage site (Pugsley, A. P.. 1993. The complete general secretory pathway in Gram-negative bacteria. Microbiol. Rev. 57:50-108) contributed toward reaching the minimum score of three.
- (c) A short stretch of hydrophilic amino acids greater than or equal to 1, usually lysine or arginine, following the N-terminal methionine (Pugsley, A. P., 1993. The complete general secretory 35

WO 99/28475 PCT/IB98/01939

93

pathway in Gram-negative bacteria. Microbiol. Rev. 57:50-108) contributed toward reaching the minimum score of three.

A list of ORFs in the *Chlamydia trachomatis* genome encoding putative lipoproteins is set forth above in the specification.

5

LPS-Related ORFs of Chlamydia trachomatis

Lipopolysaccharide (LPS) is an important major surface antigen of Chlamydia cells. Monoclonal antibodies (Mab) directed against LPS of Chlamydia pneumoniae have been identified that can neutralize the infectivity of Chlamydia pneumoniae both in vitro and in vivo (Peterson et al. 1988). Similar results are expected utilizing monoclonal antibodies against LPS of Chlamydia trachomatis. LPS is composed of lipid A and a core oligosaccharide portion and is phenotypically of the rough type (R-LPS) (Lukacova, M., Baumann, M., Brade, L., Mamat, U., Brade, H. 1994. Lipopolysaccharide Smooth-Rough Phase Variation in Bacteria of the Genus Chlamydia. Infect. Immun. June 62(6):2270-2276.) The lipid A component is composed of fatty acids which serve to anchor LPS in the outer membrane. The core component contains sugars and sugar derivatives such as a trisaccharide of 3-deoxy-D-manno-octulosonic acid (KDO) (Reeves, P.R., Hobbs, M., Valvano, M.A., Skurnik, M., Whitfield, C., Coplin, D., Kido, N., Klena, J., Maskell, D., Raetz, C.R.H., Rick, P.D. 1996. Bacterial Polysaccharide Synthesis and Gene Nomenclature pp. 10071-10078, Elsevier Science Ltd.). The KDO gene product is a multifunctional glycosyltransferase and represents a shared epitope among the Chlamydia. For a review of LPS biosynthesis see, e.g., Schnaitman, C.A., Klena, J.D. 1993. Genetics of Lipopolysaccharide Biosynthesis in Enteric Bacteria. Microbiol. Rev. 57:655-682.

A text search of the ORF Blastp results identified several genes that are involved in Chlamydial LPS production with a P score less than e⁻¹⁰. The following key-terms were used in the text search: KDO, CPS (Capsular Polysaccharide Biosynthesis), capsule, LPS, rfa, rfb, rfc, rfe, rha, rhl, core, epimerase, isomerase, transferase, pyrophosphorylase, phosphatase, aldolase, heptose, manno, glucose, lpxB, fibronectin, fibrinogen, fucosyltransferase, lic, lgt, pgm, tolC, rol, ChoP, phosphorylcholine, waaF, PGL-Tb1. A list of ORFs in the *Chlamydia trachomatis* genome encoding putative polypeptides involved in LPS biosynthesis is set forth above in the specification.

30

20

Type III And Other Secreted Products

Type III secretion enables gram-negative bacteria to secrete and inject pathogenicity proteins into the cytosol of eukaryotic host cells (Hueck, C. J., 1998. Type III Protein Secretion Systems in Bacterial Pathogens of Animals and Plants. In Microbiology and Molecular Biology Reviews. 62:379-433.) These secreted factors often resemble eukaryotic signal transduction factors,

thus enabling the bacterium to redirect host cell functions (Lee, C.A., 1997. Type III secretion systems: machines to deliver bacterial proteins into eukaryotic cells? Trends Microbiol. 5:148-156.)

In an attempt to corrupt normal cellular functions, Chlamydial pathogenicity factors injected into the host cytosol will nonetheless, as cytoplasmic constituents be processed and presented in the context of the Major Histocompatibility Complex (MHC class I). As such, these pathogenicity proteins represent MHC class I antigens and will play an important role in cellular immunity. Also included in this set are secreted non-type III products that may play a role as vaccine components.

A text search of the ORF Blastp results identified genes that are involved in *Chlamydia trachomatis* protein secretion with a P score less than e⁻¹⁰. The following key-terms were used in the text search in an effort to identify surface localized or secreted products: Yop, Lcr, Ypk, Exo, Pcr, Pop, Ipa, Vir, Ssp, Spt, Esp, Tir, Hrp, Mxi, hemolysin, toxin, IgA protease, cytolysin, tox, hap, secreted and Mip.

Chlamydia trachomatis ORFs that did not meet the above keyword search criteria, but have homologs in Chlamydia pneumoniae that do meet the search criteria are included herein. The Chlamydia pneumoniae genome (French patent application No. 97-14673, filed 21 November 1997) was analyzed using the above search criteria and a number of ORFs were identified. These Chlamydia pneumoniae ORFs were tested against the Chlamydia trachomatis genome using Blastp. Any Chlamydia trachomatis ORF with a Blastp P value < e⁻¹⁰ against a Chlamydia pneumoniae homolog, identified using the above search criteria, was included. A list of ORFs in the Chlamydia trachomatis genome encoding putative secreted proteins is set forth above in the specification.

Chlamydia trachomatis RGD Recognition Sequence

Proteins that contain Arg-Gly-Asp (RGD) attachment site, together with integrins that serve as their receptor constitute a major recognition system for cell adhesion. The RGD sequence is the cell attachment site of a large number of adhesive extracellular matrix, blood, and cell surface proteins and nearly half of the known integrins recognize this sequence in their adhesion protein ligands. There are many RGD containing microbial proteins such as the penton protein of adenovirus, the coxsackie virus, the foot and mouth virus and pertactin, a 69 kDa (kilodalton) surface protein of Bordetella pertussis, that serve as ligands through which these microbes bind to integrins on the cell surfaces and gain entry into the cell. The following provides evidence supporting the importance of RGD in microbial adhesion:

a) The adenovirus penton base protein has a cell rounding activity and when penton base was expressed in *E. coli*, it caused cell rounding and cells adhered to polystyrene wells coated with the protein. Mutant analysis showed that both these properties required an RGD sequence. Virus mutants with amino acid substitutions in the RGD sequence, showed much less adherence to HeLa S3

cells, and also were delayed in virus reproduction (Bai, M., Harfe, B., and Freimuth, P. 1993. Mutations That Alter an RGD Sequence in the Adenovirus Type 2 Penton Base Protein Abolish Its Cell-Rounding Activity and Delay Virus Reproduction in Flat Cells. J. Virol. 67:5198-5205).

b) It has been shown that attachment and entry of coxsackie virus A9 to GMK cells were dependent on an RGD motif in the capsid protein VP1. VP1 has also been shown to bind ανβ3 integrin, which is a vitronectin receptor (Roivainen, M., Piirainen, L., Hovi, T., Virtanen, I., Riikonen, T., Heino, J., and Hyypia, T. 1994. Entry of Coxsackievirus A9 into Host Cells: Specific Interactions with ανβ3 Integrin, the Vitronectin Receptor Virology, 203:357-65).

10

- c) During the course of whooping cough, *Bordetella pertussis* interacts with alveolar macrophages and other leukocytes on the respiratory epithelium. Whole bacteria adheres by means of two proteins, filamentous hemagglutinin (FHA) and pertussis toxin. FHA interacts with two classes of molecules on macrophages, galactose containing glycoconjugates and the integrin CR3. The interaction between CR3 and FHA involves recognition of RGD sequence at the positions 1097-1099 in FHA (Relman, D., Tuomanen, E., Falkow, S., Golenbock, D. T., Saukkonen, K., and Wright, S. D. "Recognitition of a Bacterial Adhesin by an Integrin: Macrophage CR3 Binds Filamentous Hemagglutinin of Bordetella Pertussis." Cell, 61:1375-1382 (1990)).
- d) Pertactin, a 69 kDa outer membrane protein of *Bordetella pertussis*, has been shown to promote attachment of Chinese hamster ovary cells (CHO). This attachment is mediated by recognition of RGD sequence in pertactin by integrins on CHO cells and can be inhibited by synthetic RGD containing peptide homologous to the one present in pertactin (Leininger, E., Roberts, M., Kenimer, J. G., Charles, I. G., Fairweather, N., Novotny, P., and Brennan, M. J. 1991. Pertactin, an Arg-Gly-Asp containing *Bordetella pertussis* surface protein that promotes adherence of mammalian cells Proc. Natl. Acad. Sci. USA, 88:345-349).
- e) The RGD sequence is highly conserved in the VP1 protein of foot and mouth disease virus (FMDV). Attachment of FMDV to baby hamster kidney cells (BHK) has been shown to be mediated by VP1 protein via the RGD sequence. Antibodies against the RGD sequence of VP1 blocked attachment of virus to BHK cells (Fox, G., Parry, N. R., Barnett, P. V., McGinn, B., Rowland, D. J., and Brown, F. 1989. The Cell Attachment Site on Foot-and-Mouth Disease Virus Includes the Amino Acid Sequence RGD (Arginine-Glycine-Aspartic Acid) J. Gen. Virol., 70:625-637).

It has been demonstrated that bacterial adherence can be based on interaction of a bacterial adhesin RGD sequence with an integrin and that bacterial adhesins can have multiple

binding site characteristic of eukaryotic extracellular matrix proteins. RGD recognition is one of the important mechanisms used by microbes to gain entry into eukaryotic cells.

The complete deduced protein sequence of the Chlamydia trachomatis genome was searched for the presence of RGD sequence. There were a total of 38 ORFs that had one or more RGD sequences. Not all RGD containing proteins mediate cell attachment. It has been shown that RGD containing peptides that have proline immediately following the RGD sequence are inactive in cell attachment assays (Pierschbacher & Ruoslahti. 1987. Influence of stereochemistry of the sequence Arg-Gly-Asp-Xaa on binding specificity in cell adhesion. J. Biol. Chem. 262:17294-98). ORFs that had RGD, with proline as the amino acid following the RGD sequence were excluded from the list. Also, RGD sequence may not be available at the surface of the protein or may be present in a context that is not compatible with integrin binding. Since not all RGD-containing proteins are involved in cell attachment, several other criteria were used to refine the list of RGD-containing proteins. A list of ORFs in the Chlamydia trachomatis genome encoding polypeptides with RGD recognition sequence(s) is set forth above in the specification.

15

25

Non-Chlamydia pneumoniae ORFs

Chlamydia trachomatis ORFs were compared to the ORFs in the Chlamydia pneumoniae genome (French patent application No. 97-14673, filed 21 November 1997) using Blastp. Any Chlamydia trachomatis ORF with a Blastp «P» value greater than e⁻¹⁰ (i.e. >e⁻¹⁰) against Chlamydia pneumoniae ORFs are included in this section. A list of ORFs in the Chlamydia trachomatis genome which are not found in Chlamydia pneumoniae is set forth above in the specification.

Cell Wall Anchor Surface ORFs

Many surface proteins are anchored to the cell wall of Gram-positive bacteria via the conserved LPXTG motif (Schneewind, O., Fowler, A., and Faull, K.F. 1995. Structure of the Cell Wall Anchor of Surface Proteins in *Staphylococcus aureus*. Science 268:103-106). A search of the proteins encoded by the *Chlamydia trachomatis* ORFs was done using the motif LPXTG. A list of ORFs in the *Chlamydia trachomatis* genome encoding polypeptides anchored to the cell wall is set forth above in the specification.

ECACC Deposits

Samples of *Chlamydia trachomatis* were deposited with the European Collection of Cell Cultures (ECACC), Salisbury, Wiltshire SP4 OJG, UK on November 26, 1998 and assigned the provisional accession number 98112618. Cells can be grown, harvested and purified, and DNA can

WO 99/28475 PCT/IB98/01939

97

be prepared as discussed above. In order to enable recovery of specific fragments of the chromosome, one can run targeted PCR reactions, whose amplification products can then be sequenced and/or cloned into any suitable vector, according to standard procedures known to those skilled in the art.

In addition, a pool of clones covering the *Chlamydia trachomatis* genome was deposited with the ECACC on November 26, 1998 and assigned provisional accession number 98112617. The pool of clones contains a series of clones, which when taken together, cover the whole chromosome, with a redundancy of slightly more than ten. The total number of clones in the sample is 13,572.

Table 4 lists groups of oligonucleotides to be used to amplify each of ORFs 2-1197 according to standard procedures known to those skilled in the art. Such oligonucleotides are listed as SEQ ID Nos. 1198 to 5981. For each ORF, the following is listed: one forward primer positioned 2,000 bp upstream of the beginning of the ORF; one forward primer positioned 200 bp upstream of the beginning of the ORF; one reverse primer positioned 2,000 bp downstream at the end of ORF, which is 2,000 bp upstream of the end site of the ORF on the complementary strand; and one reverse primer 200 bp downstream at the end of ORF, which is 200 bp upstream of the end site of the ORF on the complementary strand. The corresponding SEQ ID Nos. for the primers are listed in Table 4, where Fp is the proximal forward primer; Fd is the distal forward primer; Bp is the proximal reverse primer; and Bd is the distal reverse primer. The positions of the 5' ends of each of these primers on the nucleotide sequence of SEQ ID No. 1 are shown in Table 5.

The present invention is not to be limited in scope by the specific embodiments described herein, which are intended as single illustrations of individual aspects of the invention, and functionally equivalent methods and components are within the scope of the invention. Indeed, various modifications of the invention, in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

20

All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

	% H	37	5	40	46	36	3	36	43	42	46		38	40	45	ő	n n	47	44	44		9	37	66
	Score	0.10	۲/۲	285	552	366	202	174	157	318	324		152	209	367	,	410	324	577	223		98 	642	2214
	Species		Chlamydia psittaci	Haemophilus influenzae	Decharichia COLI	ESCITE LOTTE COLL	Haemophilus influenzae	Staphylococcus carnosus	Bacillus subtilis	Synechococcus sp.	ı	tuberculosis	Methanococcus jannaschii	Synechocystis sp.	Haemophilus influenzae	- 1	Oryctolagus cuniculus	Saccharopolyspora erythraea	Bacillus subtilis	Escherichia coli		Borrelia burgdorferi	Shiqella flexneri	Chlamydia trachomatis
	ID		U72499	U32786	200000	AEOOOTES	U32770	X78084	AF008220	D28752	280108	9	U67605	D90913	U32691		U75284	L38646	M97391	U18997		956080	D11024	X52175
TABLE 1	Homology	putative	putative 98 kDa outer	lipid A disaccharide	syllulerase (Tpha)	ļ	D-alanine permease (dagA)	signalpeptidase II	Vtel	169	OKF 108	diskilowii	hypothetical protein (SP: P39587)	rena methylase	hypothetical		neutral amino acid transporter B0.	dihydrolipoamide	branched chain alpha-keto	328	putative	putative outer membrane	Process	dnak like protein (AA 1-660)
	stop	208	505	3242		5126	6619	8082	8501	4000	6/68	10430	11254	11916	13324		14413	15019	15969	16501	16138	17417	10137	20814
	begin	501	3276	5068		6400	7977	8582	1000	2000	9440	9828	10367	11215	12068		13532	14807	14932	15995	16467	18190		22202
	ORF	ORF2	ORF3	ORF4		ORF5	ORF6	ORF7	000	ORFO	ORF9	ORF10	ORF11	0.100	ORF13		ORF14	ORF15	ORF16	71200	ORF18	ORF19		ORF21

1%	88	66	86	87	66	66	66		46			45		T	32	4			T
Score	558	503	580	373	1999	3044	1298		786			126			175	245			+
Species	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis		Synechocystis sp.			Bartonella bacilliformis			Saccharomyces cerevisiae	Caenorhabditis elegans							
ΙD	122180	M62819	125105	L25105	L25105	L25105	L25105		D64004			L46591			U18917	271261			
Homology	ORF, 82 kDa protein	heat shock protein	GrpE-like protein	GrpE-like protein	has homology to putative heat shock proteins of Bacillus subtilis and Clostridium acetobutylicum; ORFA; putative	aminoacyl-tRNA synthetase	ORFB; putative	putative	hypothetical protein	putative	putative	putative	putative	putative	Yer156cp	F21C3.3	putative	putative	putative
stop	22153	22478	22824	23110	23394	24641	27710	27725	28740	30032	30520	31780	31800	33314	35027	35359	35919	36996	37013
pegin	22602	22804	23183	23394	24569	26383	26640	28780	29957	30721	31281	31436	33356	33901	34116	34988	35167	35923	37810
ORF	ORF22	ORF23	ORF24	ORF25	ORF26	ORF27	ORF28	ORF29	ORF30	ORF31	ORF32	ORF33	ORF34	ORF35	ORF36	ORF37	ORF38	ORF39	ORF40

\dashv	84	4		43			42			-	47			_	98					37		-	. 4	44
Score	529	192		663	681	959	755				892				142		462	801	154	355			350	290
Species	Bacillus subtilis	Escherichia coli		Mycobacterium tuberculosis	Chlamydia trachomatis	Chlamydia trachomatis	Flaveria bidentis				Pseudomonas aeruginosa				Nicotiana tabacum		Synechocystis sp.	Synechocystis sp.	Escherichia coli	Methanococcus jannaschii			Pseudomonas syringae pv. tabaci	Methanococcus
QI .	AF008220	X67753		298209	L40822	L40822	L40958				M33223				L32794		D90911	X67516	M13045	U67500			U47017	. U67476
Homology	DAPH synthase-chorismate mutase	arginine binding protein	putative	hypothetical protein MTCY154.05c	phophoglucoisomerase-like protein	phophoglucoisomerase-like protein	NADP-malate dehydrogenase	putative	putative	putative	membrane protein (arcD)	putative	putative	putative	dehydroguinate	dehydratase/shikimate dehydrogenase	3-dehydroquinate synthase	chorismate synthase	shikimate kinase II	5-enolpyruvylshikimate 3- phosphate synthase	putative	putative	dihydrodipicolinate reductase	aspartate-semialdehyde
stop	39085	39927	40756	42007	43116	43802	45227	45275	45975	46506	46882	48178	48630	50099	50925		52348	53466	54595	55031	56084	58235	59181	60195
begin	38207	39151	39923	40760	42175	42999	44211	46072	46340	46895	47955	48585	50072	50710	52439		53484	54536	55086	56350	55659	56847	58423	59185
ORF	ORF41	ORF42	ORF43	ORF44	ORF45	ORF46	ORF47	ORF48	ORF49	ORF50	ORF51	ORF52	ORF53	ORF54	ORFSS		ORF56	ORF57	ORF58	ORF59	ORF60	ORF61	ORF62	ORF63

81	41	42		42				4		38	43	43	33				8		75					38		40	48	
Score	312	345		148				733		156	306	272	Co	2			283		1447	•				495		400	1927	
Species	Escherichia coli	Helicobacter pylori		Bacillus subtilis				Bacillus subtilis		Mycobacterium tuberculosis	Bacillus subtilis	Calothrix PCC7601	Haemonhilus influenzae				Bacillus subtilis		Escherichia coli					Haemophilus influenzae		Synechocystis sp.	Arabidopsis thaliana	
a	900000	AE000609		Y14084				D26185		294752	D26185	X10305	U32727				M96343	10000	AECOOTE 84					U32750		D64001	U88087	
Homology	aspartokinase III	dihydrodipicolinate synthetase (dapA)	putative	hypothetical protein	putative	putative	putative	unknown	putative	KsgA	high level kasgamycin resistance	polypeptide deformylase	protein translocation	protein, low temperature (secG)	putative	putative	homologous to unidentified E. coli protein	900	יייייייייייייייייייייייייייייייייייייי	por identical (14 gaps) to 525 residues of an approx.	te.	SW: P44808	putative	integrase-recombinase	protein (xerC)	hypothetical protein	LON protease homolog	putative
stop	61483	62353	63141	63983	64071	64656	64609	67269	68873	69233	69721	70455	71006		98014	73497	74876	75502	3000				77299	77145		78154	79878	83271
begin	60188	61496	62500	63396	64628	64285	64944	65347	67656	68877	69212	69958	70701		73191	74900	75463	77124	1				77000	78095		79065	81971	82639
ORF	ORF64	ORF65	ORF66	ORF67	ORF68	ORF69	ORF70	ORF71	ORF72	ORF73	ORF74	ORF75	ORF76		ORF77	ORF78	ORF79	ORFRO	200				ORF81	ORF82		ORF83	ORF84	ORF85

H %	42						32	8	35		3 2	- [કુ	40	4	42	94	37	49		53	84	88	
Score	822						128	671	120		542		326	487	2090	319	2411	494	471		634	558	300	
Species	Salmonella typhimurium						Bacillus subtilis	Bacillus stearothermophilus	Bacillus subtilis		Bacillus subtilis		Helicobacter pylori	Helicobacter pylori	Thermus thermophilus	Helicobacter pylori	Chlamydia trachomatis	Synechocystis sp.	Bacillus subtilis		Haemophilus influenzae	Bacillus subtilis	Arabidopsis thaliana	
£	U58360						X12832	U12340	X17014		X06803		AE000583	AE000583	D49911	AE000583	U83196	D90903	D84432		U32723	L29475	U18969	
Homology	DnaJ	putative	putative	putative	putative	putative	Hpr protein	PTS enzyme I	ORF107	putative		polymerase III	excinuclease ABC subunit A (uvrA)	excinuclease ABC subunit A (uvrA)	UvrA	excinuclease ABC subunit A (uvrA)	pyruvate kinase	hypothetical protein	1	putative	exonuclease VII, large subunit (xseA)	triose phosphate isomerase	phosphoribosylanthranilate isomerase	
aton	84850	86921	87313	87805	88747	89265	89732	91447	91435	91745	92344		93361	94071	94628	98113	98741	100337	101323	102210	102726	104254	105894	
hegin	83792	84876	88650	87440	88400	88717	89355	89735	91749	92392	93138		94134	94637	98299	98715	100228	101347	102210	102485	104315	105075	105259	
AGO	ORF86	ORF87	ORF88	ORF89	ORF90	ORF91	ORF92	ORF93	ORF94	ORF95	ORF96		ORF97	ORF98	08599	ORF100	ORF101	OBF102	ORF103	ORF104	ORF105	ORF106	ORF107	

% H				100	37	9	3 2	38	62	61	20	20	4			T	45	48		×	38	32		7
Score				2007	313	7.43	528	143	254	2675	3486	677	121				1062	790		188	110	. 68		1762
Species				Chlamydia trachomatis	Haemophilus influenzae	Doc'11112 21112		Thermotoga maritima	Synechocystis PCC6803	Staphylococcus aureus	Haemophilus influenzae	Homo sapiens	Homo sapiens				Gallus gallus	Haloferax volcanii		Enterococcus hirae	Enterococcus hirae	Enterococcus hirae		Synochocyetie
ដ				L22216	U32754	D12202	Z11839	Z11839	X53178	X64172	U32733	L19437	U67611				U22077	X79516		D17462	X76913	X76913		D64006
Homology	putative	putative	putative	elongation factor Tu	transcription antitermination protein	(nusg)	protein	ribosomal protein L10	rpl12 (AA 1-128)	DNA-directed RNA polymerase beta chain	DNA-directed RNA polymerase beta' chain (rpoC)	transaldolase	transaldolase	putative	putative	putative	Al isoform of vacuolar H+- ATPase subunit A	membrane ATPase	putative	Na+ -ATPase subunit I	v-type Na-ATPase	v-type Na-ATPase	putative	valy1-tRNA synthetase
stop	108955	109013	109704	112520	113463	113994	114604	115253	115676	119795	124010	124988	125106	125536	126930	127785	129714	131033	131629	133156	133584	133999	134508	137454
begin	108665	109459	110366	111330	112915	113566	114020	114720	115362	116022	119823	124065	124873	126261	126328	127138	127924	129720	131018	131834	133075	133625	133861	134638
ORF	ORF109	ORF110	ORF111	ORF112	ORF113	ORF114	ORF115	ORF116	ORF117	ORF118	ORF119	ORF120	ORF121	ORF122	ORF123	ORF124	ORF125	ORF126	ORF127	ORF128	ORF129	ORF130	ORF131	ORF132

%I	44			33	23	33		4	26	53	3	3	44		43				1,	Ť	49	£5	53		0,0	ŝ		
Score	452			282	1113	356		741	625	700	*0/	277	168		169				000	292	555	986	1535			66		
Species	がいたのかっていい。	tuberculosis		Yersinia pestis	Bacillus subtilis	Bacillus subtilis		Streptococcus pneumoniae	Caenorhabditis elegans		Helicobacter pylori	Mycobacterium tuberculosis	Escherichia coli		Recherichia coli	-			2 d d	Haemophilus influenzae	Escherichia coli	Bacillus subtilis	Darilling cubtilis			Bacillus subtilis		
a	000100	7,75,70,7		U22968	D26185	D64116		Z47210	D12984		AE000604	296072	U18997		700071	166010				U32702	AE000213	U02604	A02001	002604		Y08559		
Homology		PknD	putative	norphobilinogen deaminase		ORF3	putative	unknown		dismutase precursor	acetyl-CoA carboxylase beta subunit (accD)	Dut	enzyme ITANtr		purarive	enzyme IIANtr	putative	putative	putative	hypothetical	hypothetical protein in purB	ClpC adenosine	tripnospnacase	ClpC adenosine triphosphatase	putative	Unknown	putative	
1	goag	140276	140335	741077	111780	143128	144393	146326	147078		148075	148549	149027	10001	149305	149708	150911	151004	151999	153352	153997	153984		155231	157525	158955	159961	
	pegin	137442	140733	141799	000000	143240	143923	144548	146413		147140	148115	149524	£700£1	149000	149187	149712	152044	152664	152900	153389	155276		156544	156806	157489	159104	
	ORF	ORF133	OPF134	Oner of	ORFISS	ORF135	ORF 137	ORF139	ORF140		ORF141	ORF142	2,500	UKF 143	ORF144	ORF145	ORF146	ORF147	ORF148	ORF149	ORF150	ORF151		ORF152	ORF153	ORF154	ORF155	

æ H	34	20	83	53	စ္က	35		98		ж Ж			9	94	43		20	33	42	20
Score	256	173	371	452	93	154		96		66				373	545		1758	580	148	795
Species	Helicobacter pylori	Arabidopsis thaliana	Bacillus subtilis	Bacillus subtilis	Escherichia coli	Haemophilus influenzae		Synechocystis sp.		Rhodobacter sphaeroides			- 1	Helicobacter pylori	Staphylococcus aureus		Homo sapiens	Escherichia coli	Saccharomyces cerevisiae	Caenorhabdítis elegans
Ð	AE000536	AF007270	Y13937	AF008220	D90888	U32728		D90902		AJ000977				AE000645	D89066		U47025	X16931	X86470	277659
Homology	H. pylori predicted coding region HP0152	contains similarity to DNA polymerase III, alpha chain (SP:P47277)	putative Ptc1 protein	Nifs2	similar to [SwissProt Accession Number P37908]	hypothetical	putative	regulatory protein for beta- lactamase	putative	prolipoprotein diacylglyceryl transferase	putative	putative	putative	60 kDa inner-membrane protein	DnaA	putative	glycogen phosphorylase B	glycogen phosphorylase (AA 1 - 790)	unknown	F23B12.5
stop	180631	181398	183656	184786	184796	186000	186749	187809	188798	190352	190510	191786	192464	193183	194630	194690	197031	197635	198208	197668
heatn	181398	182594	182895	183665	186007	186848	187270	187426	189481	189693	190235	190785	191790	192392	193254	195046	195184	197018	197762	198963
400	ORF176	ORF177	ORF178	ORF179	ORF180	ORF181	ORF182	ORF183	ORF184	ORF185	ORF186	ORF187	ORF188	ORF189	ORF190	ORF191	ORF192	ORF193	ORF194	ORF195

18	48	31	8	£3		38			31	9	SS.	48	51	25	34	T	63	43
Score	856	170	302	127		577			83	334	706	522	616	220	150		852	231
Species	Arabidopsis thaliana	Porphyra purpurea	Thiobacillus ferrooxidans	Clostridium magnum		Escherichia coli			Brucella abortus	Synechocystis sp.	Escherichia coli	Bacillus subtilis	Bacillus subtilis	Haemophilus influenzae	Rattus norvegicus		Chlamydia psittaci	Chlamydia psittaci
ξĪ	U09137	U38804	U81808	L31844		U70214			U51683	D90916	M77744	U59433	U59433	U32701	J02934		AF017105	AF017105
Homology	pyruvate dehydrogenase El beta subunit	pyruvate dehydrogenase El component, alpha subunit	pyruvate dehydrogenase complex El alpha subunit	TPP-dependent acetoin dehydrogenase alpha-subunit	putative	UDP-3-0-[3-hydroxymyristoy1]	acyltransferase	putative	OMP1 precursor	recombination protein	beta-ketoacyl-acyl carrier protein synthase III	malonyl-CoA:Acyl carrier protein transacylase	3-ketoacyl-acyl carrier protein reductase	acyl carrier protein (acpP)	protein kinase type II regulatory subunit (, EC 2.7.1.37)	putative	unknown	inclusion membrane protein C
stop	198962	199941	200266	200585	202377	202380		203471	204059	206811	208528	209471	210214	210816	210883	211374	212875	214168
begin	199957	200327	200685	200962	201169	203441		203998	206449	207425	207506	208545	209471	210586	211332	212978	214134	214710
ORF	ORF196	ORF197	ORF198	ORF199	ORF200	ORF201		ORF202	ORF203	ORF204	ORF205	ORF206	ORF207	ORF208	ORF209	ORF210	ORF211	ORF212

# I	47	02	9									8	33	46	25	42	36		48	စ္တ	35	
Score	181	1341	1027									,	619	530	334	96	321		274	246	740	٦. ٢.
Species	Chlamydia psittaci	Chlamydia psittaci	Chlamydia psittaci										Chlamydia trachomatis	Bacillus subtilis	Methanococcus jannaschii	Saccharomyces cerevisiae	Bacillus firmus		Helicobacter pylori	Escherichia coli	Tottocomme Jostic	Lactococcus ractis
A	AF017105	AF017105	AF017105										057090	D84432	U67467	U43834	U61168		AE000602	AE000232	0001	AFOUSOBB
Homology	inclusion membrane protein B	sodium-dependent transporter	amino acid transporter	putative	LAGLI-DADG endonuclease	YqfU	phenylacrylic acid decarboxylase	Ydr537cp	4-hydroxybenzoate octaprenyltransferase	putative	stationary-phase survival protein (surE)	f311; This 311 aa ORF is 22 pct identical (13 gaps) to 186 residues of an approx. 488 aa protein YACA_BACSU		GadC								
aton	214754	215236	216892	217441	218702	219009	219748	220430	221074	221541	222092	223290	223818	225171	225174	225549	225749	226769	227161	227750		228607
herin	215143	216705	217917	217088	218364	218695	219179	219891	220499	221137	221601	222472	223423	224278	225749	225334	226654	227299	227646	228457		230001
Baco	ORF213	ORF214	ORF215	ORF216	ORF217	ORF218	ORF219	ORF220	ORF221	ORF222	ORF223	ORF224	ORF225	ORF226	ORF227	ORF228	ORF229	ORF230	ORF231	ORF232		ORF233

%I	95			52	37	22	25	61	46	100	43		42	42		47	38	æ	47	31	36
Score	985			351	151	105	650	1836	410	2240	1021		1017	951		442	532	601	464	119	317
Species	Escherichia coli			Methanobacterium thermoautotrophicum	Synechocystis sp.	Escherichia coli	Pseudomonas aeruginosa	Bacillus subtilis	Bacillus subtilis	Chlamydia trachomatis	Ricinus communis		Ricinus communis	Bacillus subtilis		Lactococcus lactis	Bacillus subtilis	Bacillus subtilis	Bacillus subtilis	Borrelia burgdorferi	Bacillus subtilis
Ωī	AE000299			D88555	D90906	U28377	X82072	AF008220	AF008220	Z22659	Z32850		Z32850	D86417		L18760	M57689	M57689	M57689	AF000366	M57689
Homology	4	512 aa protein FLIC_SALMU SW: P06177	putative	orf2	hypothetical protein	ORF_0211	glutamate 1-semialdehyde 2,1 aminomutase	leucine tRNA synthetase	leucine tRNA synthetase	3-deoxy-D-manno-2- octulosonic acid (Kdo) transferase	pyrophosphate-dependent phosphofructokinase beta subunit	putative	pyrophosphate-dependent phosphofructokinase beta subunit	Yfls	putative	ATP binding protein	sporulation protein	sporulation protein	sporulation protein	oligopeptide permease homolog AII	sporulation protein
stop	230151		233006	233829	234265	234854	235227	238209	238769	240061	240313	241941	242798	244479	245924	246985	247743	248569	249766	250545	251095
begin	231074		231348	233059	233801	234282	236300	236314	238164	238769	242022	242846	244480	245897	246877	247731	248585	249420	250383	251186	252111
ORF	ORF234		ORF235	ORF236	ORF237	ORF238	ORF239	ORF240	ORF241	ORF242	ORF243	ORF244	ORF245	ORF246	ORF247	ORF248	ORF249	ORF250	ORF251	ORF252	ORF253

1%	94	35	44		-	g G	45	37	32	47	66	<u>ග</u>	100	91	100
Score	601	103	482			1925	1963	307	162	218	914	1770	403	320	2828
Species	Bacillus subtilis	Synechocystis sp.	Zymomonas mobilis			Salmonella typhimurium	Aeromonas salmonicida	Bacillus subtilis	Haemophilus influenzae	Anabaena sp.	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis
ΩI	D88802	D90905	L33777			Y07916	L47978	D26185	U32802	U14553	U83195	U83195	U15192	U15192	U15192
Homology	P. haemolytica o- sialoglycoprotein endopeptidase; P36175 (660) transmembrane	Mg2+ transporter	tRNA guanine transglycosylase	putative	putative	subunit B of DNA gyrase	DNA gyrase	unknown	replication protein (dnax)	putative isozyme of glucose- 6-P-dehydrogenase; developmentally regulated gene in heterocyst development	glucose 6-phosphate dehydrogenase	glucose 6-phosphate dehydrogenase	ORF3	ORF3	CTP synthetase
stop	252066	256718	257844	258690	259187	261604	264129	264742	265628	265631	266426	266942	268066	268205	268500
begin	253088	255153	256762	257911	258780	259193	261622	264125	264741	266416	266938	267961	268320	268510	270116
ORF	ORF254	OPF255	ORF256	ORF257	ORF258	ORF259	ORF260	ORF261	ORF262	ORF263	ORF264	ORF265	ORF266	ORF267	ORF268

ORF	begin	stop	Homology	Ð	Species	Score	1%
ORF269	270892	270095	CMP-2-keto-3-	U15192	Chlamydia trachomatis	1313	100
			deoxyoctulosonic acid				
0.00	101110	221742	מאוורוופרממפ				
OKF2/0	7/1191	271613	putative				
ORF271	272219	272932	nitrate transporter	X61625	Synechococcus sp.	300	8
ORF272	272884	273588	putative				
ORF273	274816	273596	putative				
ORF274	274821	275666	putative				
ORF275	277689	276103	ORF_£535	U28377	Escherichia coli	396	38
ORF276	278268	278816	putative				
ORF277	279771	279013	tryptophan synthase alpha subunit	M15826	Pseudomonas aeruginosa	357	37
ORF278	280777	279767	tryptophan synthetase	M91661	Coprinus cinereus	1042	62
ORF279	281603	281295	tryptophan repressor	L26582	Enterobacter aerogenes	151	35
ORF280	282104	281787	putative				
ORF281	284335	282794	putative				
ORF282	284460	284795	putative				
ORF283	284817	285674	putative				
ORF284	285637	286137	putative				
ORF285	286357	286677	putative				
ORF286	286681	287898	hypothetical protein	U88070	Chlamydia psittaci	66	35
ORF287	288127	289227	COME ORF1	D64002	Synechocystis sp.	90	94
ORF288	289744	290679	hypothetical protein	U88070	Chlamydia psittaci	246	36
ORF289	290828	291535	putative				
ORF290	291514	292230	endonuclease	U09868	Escherichia coli	160	37
ORF291	292326	293048	putative				
ORF292	293330	294853	putative				
ORF293	295684	295010	glutamine transport ATP- binding protein Q	U67524	Methanococcus jannaschii	407	38
ORF294	296336	295692	H. influenzae predicted coding region HI1555	U32830	Haemophilus influenzae	134	37
ORF295	297238	296243	putative				

*H		00						43	44	46		55	8		56	58	52	33	55						T			T	53
Score		802						430	343	371		315	269		297	1089	208	297	483										2005
Species		Chlamydia psittaci	Į.					Bacillus subtilis	Lactobacillus fermentum	Synechococcus sp.	ı	Mycobacterium tuberculosis	Escherichia coli		Bacillus subtilis	Anabaena sp.	Bacillus subtilis	Synechocystis sp.	Bacillus subtilis										Escherichia coli
q		L35036						D84432	U97348	AB000111		Z95389	U18997		D84432	L14862	D84432	D64001	Y13937										M29364
Homology	putative	ORF2	putative	putative	putative	putative	putative	YqiZ	integral membrane protein homolog	adenylate kinase	putative	Rpsi	50s ribosomal subunit	protein L13	- 1	biotin carboxylase	Хфрм	elongation factor P	putative CfxE protein	putative	ATP-dependent protease binding subunit								
stop	318477	320142	321497	321937	322362	323140	324913	324977	325621	327203	328150	328204	328734		329292	329608	330670	331177	331721	333021	333589	333806	334361	334729	335602	335194	335903	336338	337347
begin	318947	319342	320544	321485	321901	322301	323144	325621	326268	326469	327281	328605	329066		329663	330666	331161	331731	332404	332779	333005	334357	334089	335142	335195	335673	336334	337378	339947
ORF	ORF316	ORF317	ORF318	ORF319	ORF320	ORF321	ORF322	ORF323	ORF324	ORF325	ORF326	ORF327	ORF328	1	ORF329	ORF330	ORF331	ORF332	ORF333	ORF334	ORF335	ORF336	ORF337	ORF338	ORF339	ORF340	ORF341	ORF342	ORF343

18	39	84	<u>ი</u>	66	100	6	63	41	46	4		2	42	
Score	508	140	361	1271	1051	344	344	387	492	397		606	113	
Species	Bacillus licheniformis	Streptococcus agalactiae	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia psittaci	Escherichia coli	Homo sapiens	Escherichia coli		Brassica napus	Synechocystis sp.	
ID	D88209	U49821	M31739	L12004	M31739	M31739	\$40172	AE000174	U63329	AE000209		\$60064	D90914	
Homology	Pz-peptidase	group B oligopeptidase PepB	hypA protein	heat shock protein	hypB protein	hypB protein	orf 3'of chaperonin homolog hypB [Chlamydia psittaci, pigeon strain P-1041, Peptide Partial, 98 aa]	o247; This 247 aa ORF is 51 pct identical (0 gaps) to 117 residues of an approx. 160 aa protein YPH7_CHRVI SW: P45371	mutY homolog	hypothetical 36.0 kD protein in rne-rpmF intergenic region	putative	enoyl-acyl carrier protein reductase [Brassica napus, Peptide, 385 aa]	hypothetical protein	putative
aton	341847	342022	342470	343370	344032	344225	345142	345161	346080	347940	348146	351283	351314	352245
hogin	340507	341783	342249	342597	343361	343956	344357	345934	347102	347113	350164	350423	352207	352727
200	ORF344	ORF345	ORF346	ORF347	ORF348	ORF349	ORF350	ORF351	ORF352	ORF353	ORF354	ORF355	ORF356	ORF357

%H	8		09	8	44	100	92	86	32	42	49	52	88	83	28	37	29	29	46	88	49	48	T
Score	213		577	417	1305	948	1216	3311	116	362	192	978	1631	516	2817	585	528	1362	182	1926	286	379	
Species	Bacillus subtilis		Arabidopsis thaliana	Neurospora crassa	Escherichia coli	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Bacillus subtilis	Synechocystis sp.	Pseudomonas fluorescens	Escherichia coli	Chlamydia psittaci	Haemophilus influenzae	Chlamydia psittaci	Chlamydia psittaci							
ΩI	AB001488		Z23108	D45049	D90729	U74759	U74759	U74759	Z18631	D90917	M35367	AE000219	U88070	U88070	U88070	U88070	U88070	U88070	U32776	U88070	U88070	U88070	
Homology	FUNCTION UNKNOWN, SIMILAR	PRODUCT IN E. COLI AND MYCOPLASMA PNEUMONIAE.	NADPH thioredoxin reductase	Thioredoxin Reductase (NADPH)	30S ribosomal protein S1	NusA	NusA		ORF6 gene product	tRNA pseudouridine 55 synthase	protein X	hypothetical GTP-binding protein in pth 3' region	cds1 gene product	cds2 gene product	cds2 gene product	gene	scc1 gene product	No definition line found	ribosomal protein L28 (rpL28)	hypothetical protein	hypothetical protein	hypothetical protein	putative
stop	353305		353670	354140	356672	357377	358093	360743	361121	361884	362746	362816	365195	365587	367320	368603	369081	370251	371086	372816	373529	374204	374224
begin	353709		354218	354721	354966	356700	357326	358035	360753	361162	361826	363859	364116	365198	365479	367341	368644	369088	370769	371203	373119	373614	374736
ORF	ORF358		ORF359	ORF360	ORF361	ORF362	ORF363	ORF364	ORF365	ORF366	ORF367	ORF368	ORF369	ORF370	ORF371	ORF372	ORF373	ORF374	ORF375	ORF376	ORF377	ORF378	ORF379

ж Н	8	2 2 3	51		45	51	39	35		8		45	41		35	42	40	31	51	30		96	- 6	3	ă.
Score		490	678		137	216	92	477		134		185	989		150	168	134	164	592	282		1295		1235	543
Species		Chlamydia trachomatis	Synechocystis sp.		Haemophilus influenzae	Synechocystis sp.	Haemophilus influenzae	Bacillus subtilis		Escherichia coli		Helicobacter pylori	Synechocystis sp.		Streptococcus parasanguis	Bacillus subtilis	Treponema pallidum	Cyanophora paradoxa	Treponema pallidum	Bacillus subtilis		Arabidopsis thaliana			Helicobacter pylori
B		L40838	D64000		U32702	D90914	U32780	D26185		U70214		AE000606	D64000		M26130	AF008220	U55214	U30821	U55214	AF008220		249227		X91655	AE000552
Homology	putative	corresponds to a 97 amino acid long polypeptide	methylenetetrahydrofolate dehydrogenase	putative	hypothetical	small protein	10.4	recombination protein	putative	hypothetical	putative	conserved hypothetical secreted protein	hypothetical protein	1	ORF1; putative	vtaD	Trok	putative protein of 299 amino acids	Trob	YtgA	putative	adenine nucleotide	translocase	lepA gene product	GTP-binding membrane protein (lepA)
stop	374703	376748	378737	379048	379403	379641	381470	382567	383702	383655	383949	385178	385706	386627	386872	387338	387816	388237	389173	389945	391810	393996		395354	395992
begin	376391	377062	377853	378626	379017	380009	380187	381473	382704	383945	385217	385507	386845	386127	387372	387823	388250	389169	389955	390988	391514	392410		394170	395309
ORF	ORF380	ORF381	ORF382	OBE383	ORF384	000385	ORF386	ORF387	ORF388	ORF389	ORF390	ORF391	ORF392	ORF393	ORF394	000395	ORE396	ORF397	085398	ORF399	ORF400	ORF401		ORF402	ORF403

Homology		Ω.	Species	Score
phosphogluconate dehydrogenase	ate	U30255	Homo sapiens	411
6-phosphogluconate dehydrogenase		AB006102	Candida albicans	806
tyrosyl-trna	synthetase	M13148	Bacillus caldotenax	844
whiG-Stv gene	product	X68709	Streptoverticillium griseocarneum	463
FLHA gene	product	X63698	Bacillus subtilis	134
flbF	M	M73782	Caulobacter crescentus	355
ferredoxin IV		M59855	Rhodobacter capsulatus	86
putative				
GCDE	6Ω D	D90908	Synechocystis sp.	995
putative				
YfiH	US	U50134	Escherichia coli	166
dihydrolipoamide		M27141	Bacillus subtilis	833
transsuccinylase 2.3.1.61)	inylase (odhB; EC			
alpha-ketoglu dehydrogenase	tarate	U41762	Rhodobacter capsulatus	1537
YgeR	D8	D84432	Bacillus subtilis	496
putative			the state of the s	
putative				
putative	,			
unknown	·6Z	294752	Mycobacterium tuberculosis	172 36
putative				
putative				

1%	92	98	14	36	55	3	53	3 8	3		38				3	አ	Į.	1	†	g C	2/
Score	1661	612	269	165	1220	1263	623	550	710		173				289	817		395	287	374	199
Species	Chlamydia trachomatis	Chlamydia trachomatis	Mycoplasma salivarium	Mycobacterium leprae	- 1	Synechocystis sp.	- 1	Pseudomonas aeruginosa	Helicobacter pylori		Saccharomyces cerevisiae				Escherichia coli	Schizosaccharomyces pombe		La		Haemophilus influenzae	Haemophilus influenzae
GI	L10193	M86605	D17450	L39923		D90908		D83138	AE000554		U27182				U29581	AB004537		AF005098	X72627	<u> </u>	U32705
Homology	Hc2 nucleoprotein	[karp] gene products	aminopeptidase	putative	putative	glycogen operon protein GlgX	putative	Holliday junction specific DNA helicase	deoxycytidine triphosphate deaminase (dcd)	mitative	biotin apo-protein ligase	putative	putative	putative	exonuclease V alpha-subunit	methionyl-tRNA synthetase	putative	RNAseH II	ribosomal protein L19	tRNA (guanine-N1)- methyltransferase (trmD)	tRNA (guanine-N1)- methyltransferase (trmD)
1	418647	419672	420245	421518	423043	425079	425146	426245	427817	788007	429857	430323	431787	431987	434475	434620	436272	436567	437894	438285	438986
	419531	420190	421171	421988	422486	423226	426054	426985	427248	42000	430360	730627	430637	431658	432232	436308	436574	437685	438262	439127	439339
	ORF427	ORF428	ORF429	ORF430	ORF431	ORF432	ORF433	ORF434	ORF435	0	ORF437	0000	OKF430	OBF440	ORF441	ORF442	ORF443	ORF444	OPE445	ORF446	ORF447

Homology	ΩI	86	Score
ribosomal pr (rpS16)	protein S16 U32705 Haemophilus influenzae	nfluenzae	168
signal reco protein	signal recognition particle AE000347 Escherichia colprotein	coli	865
product similar PRFA2 protein	c to E.coli Z49782 Bacillus subtilis	ilis	314
polypeptide cha factor 1 (prfA)	chain release U32830 Haemophilus inf	influenzae	708
leader peptidase	I D90904 Symechocystis	sp.	268
isoleucyl-tRNA	synthetase U04953 Homo sapiens		704
isoleucyl-tRNA	synthetase U04953 Homo sapiens		1687
putative			
product similar PhoH protein	to E. coli Z97025 Bacillus subtilis	ilis	820
CydB	Z95554 Mycobacterium tuberculosis		105
cyanide ir oxidase	insensitive terminal Y10528 Pseudomonas aeruginosa	eruginosa	388
ide	insensitive terminal Y10528 Pseudomonas aer	aeruginosa	537
APPP	AB002150 Bacillus subtilis	ilis	324
putative			:
HtrB protein	X61000 Escherichia coli	ilc	77
unknown	U87792 Bacillus subtilis	ilis	114
hypothetical	protein Z75208 Bacillus subtilis	ilis	148
putative			
putative			
putative			
PET112		Sp.	892

% H	46					8	39	98 88		38	40	35		5		8	8		숙	8	39					ļ	à
Score	1051					173	175	193		100	537	234		313			391		114	77	909						1624
Species	Moraxella catarrhalis					Chlamydia psittaci	Chlamydia psittaci	Chlamydia psittaci	- 1	Chlamydia psittaci	Chlamydia psittaci	Chlamydia psittaci	- 1	Chlamydia psittaci		- 1	Chlamydia psittaci		Chlamydia psittaci	Chlamydia psittaci	Chlamydia psittaci			-			Synechococcus PCC6301
Ωī	U49269					U72499	U65942	U72499		U65942	U72499	U72499		U72499			U72499		U65942	U72499	U72499						M31544
Homology	amidase	putative	putative	putative	putative	putative 98 kDa outer membrane protein			putative	POMP91A	putative 98 kDa outer membrane protein		membrane protein	putative outer membrane	рготетп	putative	putative 98 kDa outer membrane protein	putative	POMP90A precursor	putative 98 kDa outer membrane protein		membrane protein	putative	putative	putative	putative	branching enzyme
stop	467419	468906	469675	469826	471106	473267	473695	474527	474602	475613	476517	478665		479088		479668	479895	481496	483429	484964	487864		485222	489247	488233	490456	490507
begin	468891	469280	469349	471226	471624	471954	473252	473982	475198	476527	478640	479084		479723		480012	481466	481732	481864	483402	484898		485725	488204	488571	489440	492765
ORF	ORF472	ORF473	ORF474	ORF475	ORF476	ORF477	ODE478	OBF479	ORF480	ORF481	ORF482	ORF483		ORF484		ORF485	ORF486	ORF487	ORF488	ORF489	ORF490		ORF491	ORF492	ORF493	ORF494	ORF495

1%			4	48								82			42	4		22	T	57	હ		39	94		T	
Score			230	245								702			102	740		611		386	82		208	384	-		
Species			Bacillus subtilis	Escherichia coli								Haemophilus influenzae			Mycobacterium tuberculosis	Escherichia coli		Myxococcus xanthus		Synechocystis sp.	Haemophilus influenzae		Methanococcus jannaschii	Escherichia coli			
ΩÏ			D84432	M54884								U32781			296072	AE000219		AF013216		D64000	U32720		U67608	M15106			
Homology	putative	putative	Үдкм	xprB	putative	penicillin tolerance protein (1ytB)	putative	putative	hypothetical protein	hypothetical protein in pth- prs intergenic region	putative	fumarate hydratase	putative	fumarase	thiamine-repressed protein (nmt1)	putative	hypothetical protein (SP:P46851)	methionine amino peptidase	putative	putative	putative						
stop	492893	492737	494675	494869	495365	494872	496634	497176	498515	499239	500732	500790	501808	502692	503722	986905	507439	507649	208590	508478	510691	511527	512185	513092	513055	515244	515269
begin	492357	493744	493875	494573	494835	495174	495687	496295	497703	498280	499215	501710	502863	503675	505002	505739	666905	508404	508291	508915	509600	511039	511547	512382	514287	514789	514994
ORF	ORF496	ORF497	ORF498	ORF499	ORF500	ORF501	ORF502	ORF503	ORF504	ORF505	ORF506	ORF507	ORF508	ORF509	ORF510	ORF511	ORF512	ORF513	ORF514	ORF515	ORF516	ORF517	ORF518	ORF519	ORF520	ORF521	ORF522

£ 1				21	52	49	47	ጷ	49	76		4							52	40	47	ς 20	43	
Score				340	245	306	387	860	970	314		148							476	164	230	452,	488	
Species				Porphyromonas gingivalis	Synechocystis sp.	Pisum sativum	Spinacia oleracea	Escherichia coli	Escherichia coli	Haemophilus influenzae		Porphyra purpurea							Bacillus subtilis	Bacillus subtilis	Bacillus stearothermophilus	Mycobacterium tuberculosis	Synechococcus PCC7942	
ΩI				X95938	D90901	AF010578	U52048	U18997	U01376	U32812		U38804							X53057	275208	X16188	Z85982	U86147	
Homology	putative	putative	putative	orf150 gene product	30S ribosomal protein S15	polynucleotide phosphorylase	polyribonucleotide phophorylase	polynucleotide phosphorylase	ATP-binding protein	cell division protein (ftsH)	putative	ORF327 gene product	putative	putative	putative	putative	putative	putative	phenylalanyl-tRNA synthetase alpha subunit	phenylalany-tRNA synthetase beta subunit	ribosomal protein L20 (AA 1-119)	unknown	-N-4QD	acetylenolpyruvylglucosamine reductase
stop	515804	516422	517171	517400	518380	518822	519516	520497	520718	521886	522143	523623	525746	526078	526400	526735	526851	528292	529142	529624	530223	530737	533272	
begin	515553	515808	516476	517927	518096	518403	518923	519577	521986	522131	523495	524591	524652	525731	525939	526301	528323	528861	529723	530166	530543	531378	532370	
ORF	ORF523	ORF524	ORF525	ORF526	ORF527	ORF528	ORF529	ORF530	ORF531	ORF532	ORF533	ORF534	ORF535	ORF536	ORF537	ORF538	ORF539	ORF540	ORF541	ORF542	ORF543	ORF544	ORF545	

ORF	begin	stop	Homology	a	Species	Score	1%
ORF546	533849	533244	YtqB	AF008220	Bacillus subtilis	273	38
ORF547	534672	533944	hypothetical protein MTCY08D5.03c	292669	Mycobacterium tuberculosis	170	35
ORF548	535915	534878	ribonucleoside diphosphate reductase, beta subunit (nrdB)	AE000553	Helicobacter pylori	397	33
ORF549	539153	535956	ribonucleoside-diphosphate reductase l alpha subunit (nrdA)	AE000581	Helicobacter pylori	1447	51
ORF550	539731	540519	phosphatidylserine synthase (pssA)	AE000614	Helicobacter pylori	226	49
ORF551	540523	540969	putative				
ORF552	540906	541805	hypothetical 54.7 kD protein in udp 3' region precursor (0475)	AE000459	Escherichia coli	82	98 98
ORF553	543255	541825	Ydr430cp; CAI: 0.15	U33007	Saccharomyces cerevisiae	130	48
ORF554	544133	543222	putative				
ORF555	544565	544179	hypA gene product	X86493	Clostridium perfringens	221	46
ORF556	544762	544487	orfl gene product	X70951	Saccharomyces cerevisiae	153	38
ORF557	546423	544951	serine protease (htrA)	AE000610	Helicobacter pylori	981	46
ORF558	547480	546584	succinyl coenzyme A synthetase alpha subunit	U23408	Dictyostelium discoideum	869	63
ORF559	546789	547382	putative				
ORF560	547901	547476	putative succinyl-coA	AJ000975	Bacillus subtilis	388	55
ORF561	548634	547900	succinateCoA ligase (ADP-forming)	X54073	Thermus aquaticus flavus	498	46
ORF562	548692	549459	cell division protein (ftsY)	AE000588	Helicobacter pylori	330	46
ORF563	550385	549663	putative				

# H	40	36	45	51				8	S	 B	45		ဓွ	ļ	45	42			35		8
Score	508	353	1324	1009					245	130	519		874		594	334			203		315
Species	Escherichia coli	Haemophilus influenzae	Thermus aquaticus thermophilus	Haemophilus influenzae				- 1	F	Chlamydia psittaci	Bacillus subtilis		Escherichia coli		Cucumis sativus	Drosophila melanogaster			Mycobacterium tuberculosis		Chlamydia trachomatis
Ð	D90832	U32730	U17352	U32824					U65942	U72499	Y13937		U18997		M80571	M58465			294752		M62820
Homology	Tyrosine-specific transport protein (Tyrosine permease).	tyrosine-specific transport protein (tyrP)	L-glutamine:D-fructose-6-P amidotransferase precursor	hypothetical	putative	putative	putative	putative	POMP91A	putative 98 kDa outer membrane protein	- 1		ORF f495; orfF of ECMRED,	uses 2nd start	glycerol-3-phosphate acyltransferase	insulin-degrading enzyme	putative	putative	unknown	putative	putative heat shock protein ORF; putative
stop	550421	551797	553096	554927	556904	557314	558235	558310	559196	561150	563121	563943	566953		567966	570399	572021	572755	572731	573427	573660
begin	551611	553041	554946	556300	556524	558126	557810	559215	561349	562931	564083	563593	565379		567079	568021	571269	572519	573519	572879	574160
ORF	ORF564	ORF565	ORF566	ORF567	ORF568	ORF569	ORF570	ORF571	ORF572	ORF573	725500	STATE OF THE	ORF576		ORF577	ORF578	ORF579	ORF580	ORF581	ORF582	ORF583

1%	66	99	78	81	37	48	48	66					41	14	Γ	42	20	46	42
Score	384	176	358	393	94	695	243	5054					298	339		673	845	719	156
Species	Chlamydia trachomatis	Helicobacter pylori	Chlamydia trachomatis	Chlamydia trachomatis	Bacillus subtilis	Synechocystis sp.	Bacillus subtilis	Chlamydia trachomatis					Staphylococcus aureus	Listeria monocytogenes		Synechocystis sp.	Aquifex pyrophilus	Haemophilus influenzae	Rhodobacter sphaeroides
ΩI	M62820	AE000630	U31570	U31570	X16518	D90899	U87792	U20547					AB001896	U13165		D90909	U71154	U32691	U29587
Homology	ribosomal protein S18 homolog, putative	ribosomal protein S6 (rps6)	peptidyl-tRNA hydrolase	peptidyl-tRNA hydrolase	partial ctc gene product (AA 1-186)	glycogen (starch) synthase	phosphatidylglycerophosphate synthase	glycyl-tRNA synthetase	putative	putative	putative	putative	dnaG	DNA primase	putative	DNA mismatch repair protein	DNA mismatch repair protein	excinuclease ABC subunit C (uvrC)	exinuclease ABC subunit C
stop	574184	574446	574923	575057	575469	578023	578017	582104	582206	582811	583182	583438	583827	584299	585016	586610	587758	589408	589578
begin	574426	574781	575243	575458	575849	576545	578673	579012	582697	583122	583514	583869	584435	584967	585297	585240	586484	587786	589198
ORF	ORF584	ORF585	ORF586	ORF587	ORF588	ORF589	ORF590	ORF591	ORF592	ORF593	ORF594	ORF595	ORF596	ORF597	ORF598	ORF599	ORF600	ORF601	ORF602

*			¥			64	53	52		88	45	42				45	49	37	57	36		41
Score			117			991	375	571		1097	242	388				254	638	291	1069	196		780
Species		- [Bacillus subtilis			Haemophilus influenzae	Synechocystis sp.	Thermus aquaticus thermophilus		Bacillus subtilis	Bacillus subtilis	Escherichia coli				Oryza sativa	Thermoactinomyces intermedius	Arabidopsis thaliana	Ricinus communis	Escherichia coli		Helicobacter pylori
ΩI			X62539			U32693	906060	X70708		Y13937	U51868	L14681				U33283	X79068	X57545	L13242	U82598		AE000579
Homology	putative	putative	homologous to E.coli rnpA	putative	putative	cys-tRNA synthetase (cysS)	lysyl-tRNA synthetase	lysinetRNA ligase	putative	putative PriA protein	L-alanine - pimelyl CoA ligase	2-	acylglycerophosphoethanolami ne acyltransferase/acyl carrier protein synthetase	putative	putative	3'(2'),5-diphosphonucleoside 3'(2') phosphohydrolase	leucine dehydrogenase	inorganic pyrophosphatase	beta-ketoacyl-ACP synthase	HI0034 homolog	putative	conserved hypothetical protein
stop	589630	591272	592765	592849	593121	595637	595640	596154	597282	608009	600734	601910		603531	603757	605610	605582	607493	608031	609296	61019	612927
begin	590061	590739	592406	593145	593900	594138	596122	596864	597731	598524	601876	603523		603794	604413	604549	606619	606843	890609	609652	611860	611812
ORF	ORF603	ORF604	ORF605	ORF606	ORF607	ORF608	ORF609	ORF610	ORF611	ORF612	ORF613	ORF614		ORF615	ORF616	ORF617	ORF618	ORF619	ORF620	ORF621	ORF622	ORF623

%I	37	22		47	38	47	39	37		44	43	41	45	43
Score	244	134		93	555	448	380	538		313	221	228	543	103
Species	Mycobacterium tuberculosis	Escherichia coli		Mycobacterium tuberculosis	Enterococcus hirae	Haemophilus influenzae	Haemophilus influenzae	Bacillus subtilis		Bacillus subtilis	Escherichia coli	Mycobacterium tuberculosis	Escherichia coli	Bacillus subtilis
A	298209	211831		274024	U39788	U32794	U32793	X51419		Y14079	X51584	Z95388	X51584	AB001488
Homology	trna delta(2)- isopentenylpyrophosphate transferase	delta2- isopentenylpyrophosphate tRNA transferase	putative	unknown	D-alanine:D-alanine ligase	UDP-N-acetylmuramate-alanine ligase (murC)	transferase, peptidoglycan synthesis (murG)	spoVE gene product (AA 1-366)	putative	hypothetical protein	<pre>murD gene product (AA 1-438)</pre>	MurD	ORF-Y (AA 1-360)	PROBABLE UDP-N- ACETYLMURAMOYLALANYL-D- GLUTAMYL-2, 6-DIAMINOLIGASE (EC 6.3.2.15).
stop	612938	613692	615244	615683	615864	617510	618361	619247	620261	620420	621154	621674	622414	623570
begin	613597	613952	614315	615396	617711	618313	619338	620416	619863	621184	621690	622399	623466	624178
ORF	ORF624	ORF625	ORF626	ORF627	ORF628	ORF629	ORF630	ORF631	ORF632	ORF633	ORF634	ORF635	ORF636	ORF637

%I	33	31				딿	47		46	47	47	56	39	46		40	43	42
Score	243	136				467	278		361	460	756	436	1121	1426		416	638	283
Species	Synechocystis sp.	Thermoanaerobacter brockii				Escherichia coli	Escherichia coli		Bacillus subtilis	Bacillus subtilis	Haemophilus influenzae	Rhizobium leguminosarum	Thiobacillus ferrooxidans	Haemophilus influenzae		Bacillus subtilis	Salmonella typhimurium	Synechocystis sp.
A	X62437	U56021				U14003	D90837		273234	273234	U32783	X59956	X95571	U32805		M97208	U06779	D90912
Homology	UDP-N-acetylmuramoylalanyl-D glutamyl-2, 6- diaminopimelateD-alanyl-D- alanine ligase	chaperonin 60	putative	putative	putative	elongation factor P	AMP nucleosidase (EC	3.2.2.4).	transketolase	transketolase	transketolase 1 (TK 1) (tktA)	alanyl-tRNA synthetase	alanyl-tRNA synthetase	transcription-repair coupling factor (trcF) (mfd)	putative	uroporphyrinogen decarboxylase	putative oxygen-independent coproporphyrinogen III oxidase	oxygen independent coprophorphyrinogen III oxidase
stop	624073	626665	626900	627853	628124	628146	629801		629804	630298	630915	638084	640207	643472	640220	644495	645430	645840
begin	624918	625346	626514	626954	627822	628715	628932		630406	630960	631799	637488	638036	640221	640627	643485	644471	645394
ORF	ORF638	ORF639	ORF640	ORF641	ORF642	ORF643	ORF644		ORF645	ORF646	ORF647	ORF648	ORF649	ORF650	ORF651	ORF652	ORF653	ORF654

	2043 99			5						u i i i i i i i i i i i i i i i i i i i	u i i i i i i i i i i i i i i i i i i i	un li	u	u i i i i i i i i i i i i i i i i i i i	u	un la	un la	\(\text{\tinc{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\tint{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\tin}\text{\tinit}\xi\text{\text{\text{\text{\text{\text{\text{\text{\text{\tinit}\xitingt{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\tinitt{\text{\text{\text{\tinit}\xititt{\text{\text{\tinit}\xi\tinith{\text{\tinit}\xititt{\text{\text{\tinit}\xititt{\text{\text{\ti}\xititt{\text{\tinit}\xititt{\text{\tinit}\xititt{\text{\tinithint{\text{\tinit}\xititt{\text{\tinithtet{\text{\tinithter{\tinithter{\tinit}\tiinthint{\text{\tinithter{\tinithtet{\tit		
	trachomatis		Liacilomatis	trachomatis	trachomatis	trachomatis trachomatis 1s influenzae	rachomatis rachomatis influenzae influenzae	rachomatis rachomatis influenzae influenzae btilis	rachomatis rachomatis influenzae influenzae btilis	trachomatis trachomatis us influenzae subtilis subtilis subtilis	trachomatis us influenzae us influenzae subtilis subtilis subtilis oditis elegans	trachomatis trachomatis lus influenzae subtilis subtilis ditis elegans rium sis	chomatis chomatis nfluenzae nfluenzae ilis ilis selegans selegans	achomatis achomatis influenzae influenzae tilis tilis tilis is elegans n pylori	achomatis achomatis influenzae influenzae tilis tilis tilis tilis is elegans n pylori	achomatis achomatis influenzae influenzae tilis tilis tilis is elegans n pylori	achomatis achomatis influenzae influenzae tilis tilis tilis tilis is elegans n pylori	achomatis achomatis influenzae influenzae tilis tilis tilis bylori n nfluenzae		rachomatis rachomatis influenzae influenzae btilis btilis btilis tis elegans tis elegans tis elegans tinfluenzae influenzae thaliana es
	902 Chlamvdia								Chlamydia Haemophil Haemophil Bacillus Bacillus	Chlamydia Haemophil Haemophil Bacillus Bacillus	Chlamydia Haemophil Haemophil Bacillus Bacillus Bacillus Caenorhab	Chlamydia Haemophil Haemophil Bacillus Bacillus Caenorhab Chanchab Chanchab Chanchab Chanchab	Chlamydia Haemophil Haemophil Bacillus Bacillus Caenorhab Caenorhab Tuberculo Helicobac	Chlamydia Haemophil Haemophil Bacillus Bacillus Caenorhab Mycobacte tuberculo	Chlamydia Haemophil Haemophil Bacillus Bacillus Caenorhab Mycobacte tuberculo Helicobac	Chlamydia Haemophil Haemophil Bacillus Bacillus Bacillus Caenorhab Mycobacte tuberculo Helicobac	Chlamydia Haemophil Haemophil Bacillus Bacillus Caenorhab Caenorhab Hycobacte tuberculo Helicobac	03 003		23 25 25 25 25 25 25 25 25 25 25 25 25 25
L25078	M60902		M94254			U32702														
	phosphoprotein Hc1		1	prinomi gene product	gene	gene e ydroxy	gene produ e ydroxylase ydroxylase		tive olhydroxylase olhydroxylase	e ydroxylase ydroxylase ydroxylase B protein	tive clhydroxylase clhydroxylase clhydroxylase lieb protein	tive olhydroxylase olhydroxylase olhydroxylase lieb protein 7.4 thetical prote	tive olhydroxylase olhydroxylase olhydroxylase IIEB protein 7.4 thetical prote 180.08 anine glycine	tive olhydroxylase olhydroxylase olhydroxylase liEB protein 7.4 thetical prote 180.08 anine glycine 1):	gene produ droxylase droxylase ical protein e glycine	tive clhydroxylase clhydroxylase clhydroxylase liEB protein 7.4 thetical prote 180.08 anine glycine 1) 21ve 21ve 21ve	oxylase oxylase rotein al prote	gene produ droxylase droxylase ical protein e glycine in synthase ibE)	xylase xylase otein otein lycine synthase irolase irolase thase thase	
647109 phospho	650344 Hc1	-	651722 pCTHom1		652171 putativ															
649676 64	_		650418 65	L		+														
OKF656 6		\dashv	ORF658 6.		ORF660 6															

18	51		64		14	43	37		43	17	4	35	33			8		37		88	T							
Score	314		736		595	340	442	169	426	20,	494	150	101			708		338		277								
Species	Actinobaci 7 1118	pleuropneumoniae	Haloarcula marismortui		Transposon Tn5422	Mycobacterium tuberculosis	Escherichia coli	Paracoccus denitrificans	12-4-17-14 Cubtilia	מכייודומ פתקידונים	Homo sapiens	Helicobacter pylori	Cyanothece PCC 8801			Bacillus subtilis		Homo sapiens		Escherichia coli								
A	1127202	7077	X91007		L28104	274025	M22857	L02354	0000	D03550	M23068	AE000542	AF001780			M72718		S73498		000039								
Homology		riboriavin-specific deaminase	seryl-tRNA synthetase	putative	ATPase	unknown	rod-shape-determining protein	biotin [acetyl-CoA	Cathody taged tryanc	ORFXI3	2,3-bisphosphoglycerate	synthesis of [Fe-S] cluster (nifS)	Nifu	putative	putative	ORF 4	putative	AgX-1 antigen [human,	infertile patient, testis, Peptide, 505 aa]	L-glycerol 3-phosphate	deliyarogenase	putative						
stop	4000	670732	672447	673231	674562	675232	676463	676476		677700	679508	680502	681280	682558	683087	684465	684418	686203		687204		688360	688193	688432	689631	689846	690463	690672
begin		671241	671182	672692	673204	674612	675327	677027		678422	678717	679342	680579	681539	682554	683164	684774	684839		686197		687341	688432	689616	096689	690487	690717	691871
OBF	7	ORF676	ORF677	ORF678	ORF679	ORF680	ORF681	ORF682		ORF683	ORF684	ORF685	ORF686	ORF687	ORF688	ORF689	ORF690	ORF691		ORF692		ORF693	ORF694	ORF695	ORF696	ORF697	ORF698	ORF699

_		_	_	_	_	_	_		_	_	_											_			
1%	28	26	20			8	59	55	88	41		44	42	88	69	42		66	22	45					
Score	1818	961	1073			84	615	1183	362	809		165	155	1044	258	179		1548	713	273					
Species	Neocallimastix frontalis	Bacillus subtilis	Bacillus cereus			Helicobacter pylori	Myxococcus xanthus	Escherichia coli	Bacillus subtilis	Synechocystis sp.		Cyanidium caldarium	Bacillus firmus	Mycobacterium smegmatis	Zea mays	Streptomyces lividans		Chlamydia trachomatis	Bacillus subtilis	Micrococcus luteus					
ΩI	M59372	M96343	X98455			AE000591	AF013216	L18867	L47709	D90912		AF022186	X99401	U66081	U71123	U21192		U72715	X62539	U22181					
Homology	phosphoenolpyruvate carboxykinase	MreB protein	SNF	putative	putative	trigger factor (tig)	proteosome major subunit	ATP-dependent protease ATPase subunit	poly(A) polymerase	hypothetical protein	putative	Preprotein translocase subunit	secA	SecA	<pre>Cp-SecA; chloroplast SecA homolog</pre>	SecA	putative	phosphatidylserine decarboxylase	homologous to E.coli 50K	ultraviolet N-glycosylase/AP lyase	putative	putative	putative	putative	putative
stop	692041	693837	694942	697170	626269	700117	700895	702165	703412	705000	705604	705704	706138	706496	708078	708248	708872	710262	712763	713438	713651	714120	714834	715558	715921
begin	693837	694934	697263	698084	698392	698792	700269	700912	702183	703522	705011	706159	706521	708103	708398	708610	710278	711164	711432	712767	714232	714632	715592	715854	716937
ORF	ORF700	ORF701	ORF702	ORF703	ORF704	ORF705	ORF706	ORF707	ORF708	ORF709	ORF710	ORF711	ORF712	ORF713	ORF714	ORF715	ORF716	ORF717	ORF718	ORF719	ORF720	ORF721	ORF722	ORF723	ORF724

18	6		42		37	41	44	S S	39	41	%	28	71	55		33	43	0 00	92	8	8
Score	2049		997		164	722	477	388	805	154	607	266	854	531		115	208	2045	1269	1278	1153
Species	Chlamydia trachomatis		Haemophilus influenzae		Haemophilus influenzae	Bacillus subtilis	Escherichia coli	Caulobacter crescentus	Escherichia coli	Synechocystis sp.	Escherichia coli	Synechocystis sp.	Synechocystis sp.	Synechocystis sp.		Saccharomyces cerevisiae	Haemophilus influenzae	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis
ei ei	U83197		U32834		U32834	X56678	U00039	<u> </u>	D90811	D64004	D90811	D64004	D64004	D64004		L36940	U32688	M14738	U60196	U60196	U60196
Homology	3-phosphoglycerate kinase	putative	phosphate permease (YBR296C)	putative	H. influenzae predicted coding region HI1603	dciAD	was dppE	chromosome partitioning protein ParB	NifS protein.	hypothetical protein	Multidrug resistance protein 1 (P-glycoprotein 1).	ABC transporter subunit	ABC transporter subunit	ABC transporter subunit	putative	antiviral protein	penicillin-binding protein 2 (pbp2)	major outer membrane protein precursor	ribosomal protein S2	elongation factor Ts	UMP kinase
stop	717149	718862	718499	719782	720144	721575	722356	722397	723378	724576	725767	726538	726753	727469	728329	728759	729442	734427	735659	736504	737254
begin	718357	718500	719797	720273	720452	720613	721559	723248	724598	725763	726519	726819	727493	727984	728778	729346	732639	733246	734814	735644	736520
ORF	ORF725	ORF726	ORF727	ORF728	ORF729	ORF730	ORF731	ORF732	ORF733	ORF734	ORF735	ORF736	ORF737	ORF738	ORF739	ORF740	ORF741	ORF742	ORF743	ORF744	ORF745

%H	92		31	37			04	æ					55	T	T					40	88	49	34
Score	760		116	453			137	117					1220							172	970	409	107
Species	Chlamydia trachomatis		Listeria monocytogenes	Pseudomonas aeruginosa			Mycobacterium tuberculosis	Caulobacter crescentus					Pseudomonas aeruginosa							Bacillus subtilis	Clostridium acetobutylicum	Mycobacterium smegmatis	Mycobacterium tuberculosis
QI	U60196		U40604	X68594			Z80233	M69228					AF010151							M57676	U35453	X92503	Z74024
Homology	ribosome-releasing factor	putative	ORF3; putative 39 kDa protein	Хсро	putative	putative	unknown	putative	putative	putative	putative	putative	PscN	putative	putative	putative	putative	putative	putative	NAD(P)H:glutamyl-transfer RNA reductase	DNA gyrase subunit B	gyrA	unknown
stop	737787	738679	739740	740060	742045	742824	743306	744430	744611	744958	745561	746416	746944	748274	748965	749433	749721	750007	752503	753616	756814	758301	758446
begin	737254	737942	738838	742057	742869	743378	744298	744714	744985	745557	746412	746772	748269	748966	749426	749702	750029	752307	752913	754659	755000	756796	758691
ORF	ORF746	ORF747	ORF748	ORF749	ORF750	ORF751	ORF752	ORF753	ORF754	ORF755	ORF756	ORF757	ORF758	ORF759	ORF760	ORF761	ORF762	ORF763	ORF764	ORF765	ORF766	ORF767	ORF768

-	Spec	1 22 1	Score
SthB	U50134 Escherichia	a coli	241
putative			
putative			
3-deoxy-D-manno-octulo 8-phosphate synthetase	sonate U72493 Chlamydia	trachomatis	1350
unknown	U72493 Chlamydia tr	trachomatis	536
id buipuid alk	protein U72493 Chlamydia tr	trachomatis	1197
chlanectin coding	region M17875 Chlamydia	trachomatis	239
putative			
unknown function	n Z32530 Chlamydia trachomatis	rachomatis	1803
unknown function	Z32530 Chlamydia	trachomatis	704
RecA	U16739 Chlamydia tr	trachomatis	1753
unknown function	Z32530 Chlamydia	trachomatis	904
unknown function	Z32530 Chlamydia	trachomatis	2249
putative			
unknown	Bacillus	subtilis	486
ORF_f169	U18997 Escherichia	coli	263
DNA topoisomerase	I L27797 Bacillus	subtilis	1357
putative			
putative			
ORF_£397			0.2

%H			49		R	42			33		37		52				32	98	28	37		51	46			
Score			557		81	700			84		409		867				103	216	184	107		290	150	-		
Species			Escherichia coli		Escherichia coli	Gallus gallus	•		Rickettsia prowazekii		Vibrio alginolyticus		Bradyrhizobium japonicum				Neisseria meningitidis	Methanococcus jannaschii	Bacillus subtilis	Bacillus stearothermophilus		Escherichia coli	Mycoplasma-like	organism		
ΙD			X04581		M31792	M12105			U02878		237111		L24386				X92405	U67553	D84432	D13293		X61000	L22217			
Homology	putative	putative	exonuclease V (AA 1-1180)	putative	MreC protein	aspartate aminotransferase	precursor	putative	GreA	putative	NADH:ubiquinone	ovidoreducidase subuilly A	delta_aminolevulinic acid dehydratase	putative	putative	putative	ompR gene product	glucose-1-phosphate thymidylyltransferase	YqiD	farnesyl diphosphate synthase	putative	Orf39.9	This ORF is homologous to a	40.0 Kd hypothetical protein	In the ntrB 3' region from B. coli accession Number	X61000
stop	781552	782442	785524	786002	785546	786611		788021	787920	790609	792016		792059	794056	794957	795144	796255	797015	797365	797856	798086	797935	798416			
pegin	779321	781297	782447	785532	786580	787741		787620	790124	790160	790634		793084	793343	794046	795401	795575	796278	796979	797260	797772	798426	798925	*		
ORF	ORF792	ORF793	ORF794	ORF795	ORF796	ORF797		ORF798	ORF799	ORF800	ORF801	0000	ORFB02	ORF803	ORF804	ORF805	ORF806	ORF807	ORF808	ORF809	ORF810	ORF811	ORF812			

% I	46	35	97	97	100	59		20											38	32	6		45		48
Score	407	397	1716	973	280	775		125											150	90	2868		310	•	100
Species	Helicobacter pylori	Caenorhabditis elegans	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia pneumoniae		Chlamydia pneumoniae											Odontella sinensis	Homo sapiens	Chlamydia trachomatis		Pisum sativum		Neisseria meningitidis
ΩI	AE000633	U40707	U50732	U50732	U50732	L23921		L23921											267753	AB002334	J05546		X08611		X68068
Homology	ribosomal protein S4 (rps4)	apurinic/apyrimidinic endonuclease	mviB homolog	mviB homolog	lorf2; possible membrane- bound protein	76 kDa protein	putative	76 kDa protein	putative	30S ribosomal protein S20	KIAA0336	RNA polymerase sigma-subunit	putative	dihydropterin	pyrophosphokinase /dihydropteroate synthase	dihydropteroate synthase									
stop	799927	800029	802129	802673	803246	804220	805356	806282	808081	600608	809079	810328	812342	813522	813772	814334	814314	814396	815428	817456	819320	819713	820402		821061
begin	799301	800892	801062	802023	802851	803105	804307	805290	806453	808026	810461	811605	811725	812329	813455	813732	815213	814878	815733	816116	817608	819324	819704		820375
ORF	ORF813	ORF814	ORF815	ORF816	ORF817	ORF818	ORF819	ORF820	ORF821	ORF822	ORF823	ORF824	ORF825	ORF826	ORF827	ORF828	ORF829	ORF830	ORF831	ORF832	ORF833	ORF834	ORF835		ORF836

schii predicted U67522 egion MJ0768	M. jannaschii predicted U67522 coding region MJ0768 putative	M. jannaschii predicted U67522 coding region MJ0768
schii predicted U67522 egion MJ0768	M. jannaschii predicted U67522 coding region MJ0768 putative	822239 M. jannaschii predicted U67522 coding region MJ0768
WE OLDO	putative	
TOTOTON STORY		
merabottsm Rootao	nitrogen metabolism M58480 regulator	metabolism M58480
helicase M63176 Staphylococcus	M63176	824359 helicase M63176
helicase M63176 Staphylococcus	M63176	helicase M63176
ipa-57d gene product X73124 Bacillus	ipa-57d gene product X73124	827026 ipa-57d gene product X73124
putative		827250
hypothetical U32712 Haemophilus influenzae	hypothetical U32712	827230 hypothetical U32712
19/20 residue stretch (32- L19954 Bacillus 51) identical to N-terminal putative signal sequence of unknown, partly cloned B. subtilis gene.; putative	L19954	19/20 residue stretch (32- L19954 51) identical to N-terminal putative signal sequence of unknown, partly cloned B. subtilis gene.; putative
heat shock protein GroEL U55047 Bradyrhizobium	shock protein GroEL U55047	heat shock protein GroEL U55047
basl protein , Z34917 Hordeum vulgare	protein , Z34917 Hordeum	bas1 protein . Z34917 Hordeum
•		putative
nitative	+	832214
purative	+	832214
tein , Z34917	bas1 protein . Z34917 putative	831748 bas1 protein , Z34917 831751 putative
gene product ical sidue stretch (32- tical to N-terminal signal sequence of partly cloned B. gene.; putative ck protein GroEL	helicase helicase putative hypothetical hypothetical 19/20 residue stretch (32- 51) identical to N-terminal putative signal sequence of unknown, partly cloned B. subtilis gene.; putative heat shock protein GroEL bas1 protein putative	824359 helicase 825879 helicase 827026 ipa-57d gene product 827250 putative 827230 hypothetical 829275 19/20 residue stretch (32- 51) identical to N-terminal putative signal sequence of unknown, partly cloned B. subtilis gene.; putative 831748 bas1 protein GroEL 831751 putative
gene pro ical ical signal partly gene.; ck prote	helicase helicase helicase helicase helicase hypothetical hypothetical 19/20 residue st 51) identical to putative signal unknown, partly subtilis gene.; heat shock prote bas1 protein putative	# 823045 nitrogen metabol regulator regulator 824359 helicase 827026 ipa-57d gene pro
	823045 824359 827026 827026 827250 827230 829275 830953 831748 831751	

		Homology	A	Species	Score	₩ ₩
838699		putative				
839575 F	1	putative				
840583 pt	전	putative				
841713 pu	nď	putative				
842459 pu	nď	putative				
	put	putative				
	put	putative				
846196 put	put	putative				
843802 put	put	putative				
846217 put	put	putative				
848150 put	put	putative				
850230 puta	put	putative				
	put	putative				
853700 pute	pute	putative				
854920 puta	pute	putative				
855437 puta	puta	putative				
	puta	putative				
	puta	tive				
	puta	tive				
	puta	putative				
	pute	putative				
	put	putative				
	put	putative				
	put	putative				
863996 put	put	putative				
866248 DNA mi (mutL)	DNA (mu	DNA mismatch repair protein (mutL)	U32692	Haemophilus influenzae	206	47
866605 put	put	putative				
867732 YghT	Xđh	I	D84432	Bacillus subtilis	444	39
	put	putative			٠	
	put	putative				
871372 fim	£ίm	fimbrial assembly protein	L13865	Pseudomonas aeruginosa	181	\$

Adniciomonas campestris Acinetobacter calcoaceticus Escherichia coli
1031 1 1
1 1 1 1 1
1 1 1
1
aimoneila typnimurium
Yersinia pseudotuberculosis
Xanthomonas campestris
Pseudomonas aeruginosa
Erwinia amylovora
Saccharomyces cerevisiae
Clostridium magnum
Bacillus subtilis
Synechocystis sp.
Clostridium perfringens
Bacillus subtilis
Bacillus subtilis

18			39				43	52	47		51	86	100	92		37	40		43		20		39	29
Score			155				1974	1117	989		1339	1196	209	380		150	181		197		145		309	302
Species			Synechocystis sp.				Helicobacter pylori	Escherichia coli	Streptococcus equisimilis		Synechocystis sp.	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia psittaci		Synechocystis sp.	Staphylococcus aureus		Helicobacter pylori		Sinorhizobium meliloti		Pseudomonas aeruginosa	Synechocystis sp.
ID			D90908				AE000646	M17102	217214		D90910	X66126	L40369	L39892		D90914	248003		U94318		L13845		U67855	D90910
Homology	putative	putative	hypothetical protein	putative	putative	putative	DNA polymerase III alpha- subunit (dnaE)	UhpC protein	histidinetRNA ligase	putative	aspartyl-tRNA synthetase	mip-like protein	nods	trxA	putative	hypothetical protein	DNA polymerase III	putative	VdlD	putative	acid-inducible gene	putative	UDP-3-0-acyl-GlcNAc deacetylase	(3R)-hydroxymyristol acyl carrier protein dehydrase
stop	893808	893643	893821	894248	895050	896829	897064	900791	903876	903471	905605	906474	906945	907001	908742	909194	909584	909951	910569	910944	912261	912629	913218	913676
pegin	933326	893909	894276	894778	895892	895951	900783	902032	902659	903731	903860	905725	906493	902206	908101	908721	909198	909583	910081	910615	910948	912399	912595	913203
ORF	ORF912	ORF913	ORF914	ORF915	ORF916	ORF917	ORF918	ORF919	ORF920	ORF921	ORF922	ORF923	ORF924	ORF925	ORF926	ORF927	ORF928	ORF929	ORF930	ORF931	ORF932	ORF933	ORF934	ORF935

%I	8	42				48	43	47	48	89	49	57	62	66	100	100	100	66
Score	503	407				470	210	116	800	315	240	605	434	343	419	618	568	793
Species	Rickettsia rickettsii	Escherichia coli				Haemophilus influenzae	Synechococcus sp.	Thermotoga maritima	Mycoplasma-like organism	Mycoplasma pneumoniae	Thermotoga maritima	Haemophilus influenzae	Thermotoga maritima	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis
ΩI	L22690	X63666				U32761	AB000111	Z21677	M74770	AE000061	221677	U32761	221677	M80325	M80325	M80325	M80325	M80325
Homology	UDP-N-acetylglucosamine acyltransferase	methionyl-tRNA formyltransferase	putative	putative	putative	ribosomal protein L3 (rpL3)	50S ribosomal protein L4	ribosomal protein L23	rpl2	Mycoplasma pneumoniae, ribosomal protein S19; similar to GenBank Accession Number S36895, from M. bovis	ribosomal protein L22		ribosomal protein L16	ribosomal protein CtrL29e	ribosomal protein S17e	ribosomal protein CtrL14e	ribosomal protein CtrL24e	ribosomal protein CtrL5e
stop	914485	915136	915467	916633	916539	917627	918304	918655	919533	919829	920157	920840	921294	921514	921758	922143	922491	923035
begin	913691	914516	915144	915629	916051	916965	917612	918323	918682	919542	919723	920184	920866	921272	921510	921778	922159	922496
ORF	ORF936	ORF937	ORF938	ORF939	ORF940	ORF941	ORF942	ORF943	ORF944	ORF945	ORF946	ORF947	ORF948	ORF949	ORF950	ORF951	ORF952	ORF953

₩ H	86	6	66	8	66	66	901	88	97	86	66					14	38	9
Score	487	927	605	814	740	2254	604	646	847	1040	1735					250	258 ,	264
Species	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis					Haemophilus influenzae	Haemophilus influenzae	Helicobacter pylori
A	M80325	M60652	M80325	M80325	M80325	L25077	L33834	L33834	L33834	L33834	U83198					U32717	U32716	AE000540
Homology	ribosomal protein CtrS8e	ribosomal protein L6	ribosomal protein CtrL18e	ribosomal protein CtrS5e	ribosomal protein CtrL15e	homolog	ribosomal protein S13	ribosomal protein Sll	RNA polymerase alpha-subunit	RNA polymerase alpha-subunit	glyceraldehyde-3-phosphate dehydrogenase	putative	putative	putative	putative	crossover junction endodeoxyribonuclease (ruvC)	Holliday junction DNA helicase (ruvA)	nucleoside diphosphate kinase (ndk)
stop	923453	924032	924425	924937	925364	926760	927184	927604	928155	928759	930244	939086	931078	931666	931959	932579	933201	933621
begin	923160	923484	924048	924443	924933	925390	926819	927209	927577	928100	929222	930222	930608	931367	931549	932070	932602	933319
ORF	ORF954	ORF955	ORF956	ORF957	ORF958	ORF959	ORF960	ORF961	ORF962	ORF963	ORF964	ORF965	ORF966	ORF967	ORF968	ORF969	ORF970	ORF971

_	-	_	_																	
1%	22	36	51	41	83	40	36	42	32	89	99	44		41		42	47			
Score	186	156	1562	848	120	668	265	1334	198	882	417	755		223		260	178			
Species	Myxococcus xanthus	Mycoplasma genitalium	Pseudomonas putida	Bacillus subtilis	Helicobacter pylori	Arabidopsis thaliana	Bacillus subtilis	Bacillus caldotenax	Caenorhabditis elegans	Pseudomonas fluorescens	Deinococcus radiodurans	Oryza sativa		Bacillus subtilis		Mus musculus	Cucumis sativus			
ΩĨ	J05207	U39706	X62540	D26185	AE000610	249227	AF008220	D12982	227079	L27278	L27276	M31616		Z98682		M59288	D26106			
Homology	nucleoside 5'-diphosphate phosphotransferase (EC 2.7.4.6)	hypothetical protein (GB:U14003_297)	homologous to E.coli gidA	replicative DNA helicase	phosphatidylglycerophosphate synthase (pgsA)	adenine nucleotide translocase	putative protease	DNA polymerase	T05G5.5	The first ATG in the open reading frame was chosen as the initiation codon.	'The first GTG in the open reading frame was chosen as the initiation codon.'	ADPglucose pyrophosphorylase	putative	YlbH protein	putative	ferrochelatase	ferrochelatase	putative	putative	putative
stop	933785	933848	934539	936666	939098	940933	942068	944685	945287	946294	946676	948454	949277	949594	929056	951330	951643	952798	954264	955157
begin	933522	934546	936377	938081	938538	939329	941031	942082	944634	945287	946293	947105	948522	949277	949849	950680	951281	951788	953581	954426
ORF	ORF972	ORF973	ORF974	ORF975	ORF976	ORF977	ORF978	ORF979	ORF980	ORF981	ORF982	ORF983	ORF984	ORF985	ORF986	ORF987	ORF988	ORF989	ORF990	ORF991

Score I*	130 41		263	109 39		+	775 37														
Species	Methanosarcina barkeri	Bacillus subtilis	Helicobacter pylori	Methanococcus jannaschii			Bacillus subtilis	subtilis	subtilis nyces	ubtilis ces	ubtilis ces	ubtilis ces s aeruginosa	ubtilis ces s aeruginosa xanthus	ubtilis ces s aeruginosa xanthus	ubtilis ces s aeruginosa xanthus ubtilis	ubtilis s aeruginosa xanthus ubtilis ubtilis	s aeruginosa xanthus ubtilis ubtilis a coli	s aeruginosa xanthus ubtilis ubtilis a coli	s aeruginosa xanthus ubtilis a coli	s aeruginosa xanthus ubtilis a coli ces irmus	ces xanthus xanthus ubtilis a coli irmus ubtilis ubtilis
	X93084 Me	X56347 B	AE000548 H	U67593 M			Z75208 B										56	26	56	36	98
	.6X	XS																			
	orf4 gene product	OppB gene product	otide sase p	methylated DNA protein cysteine methyltransferase	putative	putative putative	putative putative phenylalanyl-tRNA synthetase beta subunit	putative putative phenylalanyl-tRNA synthet beta subunit putative	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown putative	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown putative putative	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown putative putative transcriptional activator	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown putative putative transcriptional activator pilA	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown putative putative transcriptional activaton pilA sensor protein	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown putative putative transcriptional activator pilA sensor protein putative	putative putative phenylalanyl-tRNA synthet beta subunit putative unknown putative transcriptional activator pilA sensor protein putative unknown unknown	putative putative phenylalanyl-tRNA synthetase beta subunit putative unknown putative transcriptional activator of pilA sensor protein putative unknown unknown unknown unknown applintergenic region	ive live subunit subunit ive wn cive cive cive cription or protei cive com chetical interger	iive iive subunit subunit iive own cive cive cive cive cive cive cive cive	iive iive subunit subunit iive own or protei own	ive ive subunit subunit subunit ive wn cive scription or protei cive own own chetical interger interger cive own con o
-	-	959312		961053	 961487																
	955754	957837	959299	961562	 962575	962575	962575 961979 964914	962575 961979 964914 964941	962575 961979 964914 964941	962575 961979 964914 964941 967023	962575 961979 964914 964941 967023 967444	962575 961979 964914 964941 967023 967444 968903	962575 961979 964914 964941 967023 967444 968903	962575 961979 964914 964941 967023 967444 968903 971806	962575 961979 964914 964941 967023 9770685 973053	962575 961979 964914 964941 967023 970685 971806 973053	962575 961979 964914 964941 967023 970685 970685 971806 973053 974546 975223	962575 961979 964914 964941 967023 970685 971806 973053 975223 976193	962575 961979 964914 964941 967023 970685 971806 971806 971806 971806 971806 971806 971806 971806 971806 971806	962575 961979 964914 964941 967023 970685 971806 971806 971806 971806 971806 971806 976523 976520	962575 961979 964914 964941 967023 977685 971806 973053 974546 975223 976520 976588
בים	ORF992	OBEGG3	ORF994	ORF995	 ORF996	ORF996 ORF997	ORF996 ORF997 ORF998	ORF996 ORF997 ORF998	ORF996 ORF997 ORF998 ORF999	ORF996 ORF997 ORF998 ORF999 ORF1000	ORF996 ORF997 ORF998 ORF999 ORF1000 ORF1001	ORF996 ORF997 ORF998 ORF1000 ORF1001 ORF1002	ORF996 ORF997 ORF999 ORF1000 ORF1001 ORF1003	ORF996 ORF997 ORF998 ORF1000 ORF1001 ORF1003 ORF1004	ORF1005 ORF1005 ORF1001 ORF1002 ORF1003 ORF1005	ORF1004 ORF1005 ORF1001 ORF1002 ORF1003 ORF1004 ORF1006	ORF996 ORF997 ORF999 ORF1000 ORF1001 ORF1003 ORF1005 ORF1006 ORF1006 ORF1006	ORF996 ORF997 ORF998 ORF1000 ORF1001 ORF1003 ORF1004 ORF1005 ORF1006 ORF1006 ORF1009	ORF996 ORF997 ORF998 ORF1000 ORF1001 ORF1003 ORF1005 ORF1006 ORF1007 ORF1009 ORF1009	ORF996 ORF998 ORF999 ORF1000 ORF1001 ORF1004 ORF1005 ORF1006 ORF1006 ORF1009 ORF1009 ORF1009	ORF996 ORF998 ORF999 ORF1000 ORF1001 ORF1004 ORF1005 ORF1006 ORF1006 ORF1009 ORF1009 ORF1010

å	52	40				38	4	88	35	20	46	49	38		38	43	T		99	75	83
Score	355	199				593	347	782	224	286	132	343	110		447	240			880 .	533	2018
Species	Bacillus subtilis	Haemophilus influenzae				Haemophilus influenzae	Synechocystis sp.			Mycobacterium leprae	Escherichia coli	Helicobacter pylori	Methanococcus jannaschii		Synechocystis sp.	Rhodobacter sphaeroides			Chlamydia psittaci	Chlamydia psittaci	Chlamydia psittaci
ΩI	D50551	U32717				U32788	D64006	D64006	D90915	U00021	AE000238	AE000627	U67577		D64000	U83136			U41759	U41759	U41759
Homology	spore coat protein CotRC	hypothetical	putative	putative	putative	UDP-N-acetylglucosamine enolpyruvyl transferase (murz)	arginyl-tRNA-synthetase	arginyl-tRNA-synthetase	hypothetical protein	No definition line found	o298; This 298 aa ORF is 33 pct identical (24 gaps) to 248 residues of an approx. 256 aa protein CDSA_ECOLI SW: P06466	conserved hypothetical protein	hypothetical protein (HI0920)	putative	protein-export membrane protein SecD	protein-export membrane protein	putative	putative	RecJ recombination protein	unknown	glutamyl-tRNA synthetase homolog
stop	978984	979331	979389	980112	981148	983598	983862	984371	668386	986046	986693	987616	987936	989163	993442	993785	993416	994262	935656	119966	998267
pegin	978619	978933	261186	979711	982116	982321	984488	985381	986103	986693	987607	988119	988253	988831	989693	993408	993835	993882	994226	980966	996885
ORF	ORF1014	ORF1015	ORF1016	ORF1017	ORF1018	ORF1019	ORF1020	ORF1021	ORF1022	ORF1023	ORF1024	ORF1025	ORF1026	ORF1027	ORF1028	ORF1029	ORF1030	ORF1031	ORF1032	ORF1033	ORF1034

18	6		96	97	42	9	66	62	88	48	42	55		44		04		
Score	504	2857	276	438	486	454	662	2147	350	113	102	1021		365		108	-	
Species	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Escherichia coli	Haemophilus influenzae	Chlamydia trachomatis	Helicobacter pylori	Spirulina platensis	Escherichia coli	Mycobacterium tuberculosis	Bacillus subtilis		Synechocystis sp.		Haemophilus influenzae		
A	M35148	M23001	M35148	M35148	D00674	M86701	211567	AE000625	221676	M23008	292774	238002		D90915		U32759		
Homology	9-kDa cysteine-rich outer membrane protein	outer membrane protein 2	15-kDa serine-rich outer membrane protein	15-kDa serine-rich outer membrane protein	ORF of prc gene (alt.)	StrA	ribosomal protein S7	translation elongation factor EF-G (fusA)	ribosomal protein S10	144 0	unknown	serine hydroxymethyltransferase	putative	ATP-dependent Clp protease proteolytic subunit	putative	diaminopimelate epimerase (dapF)	putative	putative
aton	999225	1001033	1001516	1001664	1001823	1004845	1005382	1007496	1007821	1008698	1009121	1012054	1011942	1012635	1012862	1013440	1014055	1014489
hood	998962	999375	1001211	1001392	1003721	1004459	1004990	1005391	1007486	1007802	1009426	1010534	1012397	1012042	1012593	1012811	1013456	1013977
880	ORF1035	ORF1036	ORF1037	ORF1038	ORF1039	ORF1040	ORF1041	ORF1042	ORE1043	ORF1044	ORF1045	ORF1046	ORF1047	ORF1048	ORF1049	ORF1050	ORF1051	ORF1052

ORF	pegin	stop	Homology	£	Species	Score	#H
ORF1053	1015224	1014529	hypothetical 28.1 kD protein	AE000459	Escherichia coli	263	38
			in udp-rfaH intergenic region				
ORF1054	1016002	1015145	putative				
ORF1055	1017120	1015939	conserved hypothetical	AE000579	Helicobacter pylori	428	42
			protein				
ORF1056	1017766	1017245	putative				
ORF1057	1018911	1017916	putative				
ORF1058	1019191	1018580	putative				
ORF1059	1020199	1686101	hemolysin	AE000647	Helicobacter pylori	164	33
ORF1060	1021007	1020114	unknown	295208	Mycobacterium	201	36
ORFIDE1	1021569	1021075	nitative		capercars		
ORF1062	1022411	1022097	putative				T
200			1				1
ORF1063	1023344	1023667	50S ribosomal subunit protein L21	U18997	Escherichia coli	218	43
ORF1064	1023701	1023949	50S ribosomal protein L27	U38804	Porphyra purpurea	251	8
ORF1065	1023976	1024776	ORF_£390	U18997	Escherichia coli	603	51
ORF1066	1024704	1025045	GTP-binding protein (obg)	U32769	Haemophilus influenzae	161	37
ORF1067	1025881	1024967	hypothetical protein	D90903	Synechocystis sp.	439	35
ORF1068	1026546	1025839	YcdI	AB000617	Bacillus subtilis	312	40
ORF1069	1027379	1026546	adhesion protein	D90903	Synechocystis sp.	354	35
ORF1070	1030604	1027929	putative 98 kDa outer membrane protein	U72499	Chlamydia psittaci	95	49
ORF1071	1033252	1030508	putative 98 kDa outer	U72499	Chlamydia psittaci	75	36
			membrane protein				
ORF1072	1031733	1032086	putative				
ORF1073	1037037	1033456	putative 98 kDa outer membrane protein	U72499	Chlamydia psittaci	160	46
ORF1074	1035674	1035910	putative				

ORF	ORF begin	Bţ	Hc	αI	Species	Score	% H
ORF1075	1036175	1036507	putative				

ORF	begin	stop	Homology	ΩI	Species	Score	H-8-
ORF1076	68 (com)	1036967	putative				
ORF1077	16591	16989	GutQ/KpsF Family Sugar-P Isomerase	AE001313	Chlamydia trachomatis	658	97
ORF1078	31779	31408	putative				
ORF1079	56502	56834	hypothetical protein	AE001309	Chlamydia trachomatis	284	95
ORF1080	26686	56913	hypothetical protein	AE001309	Chlamydia trachomatis	303	94
ORF1081	64748	65074	hypothetical protein (possible 357R?)	AE001309	Chlamydia trachomatis	501	100
ORF1082	73482	73195	Predicted OMP [leader (19) peptide]	AE001308	Chlamydia trachomatis	476	100
ORF1083	78482	78736	putative				
ORF1084	79803	79411	hypothetical protein	AE001307	Chlamydia trachomatis	583	98
ORF1085	82333	81959	Lon ATP-dependent protease	AE001307	Chlamydia trachomatis	607	66
ORF1086	87313	66698	hypothetical protein	AE001307	Chlamydia trachomatis	534	100
ORF1087	109929	109456	hypothetical protein	AE001305	Chlamydia trachomatis	529	86
ORF1088	111599	111351	putative				
ORF1089	112069	111734	putative				
ORF1090	112666	112911	hypothetical protein	AE001305	Chlamydia trachomatis	395	94
ORF1091	114017	113715	putative				
ORF1092	120757	120464	putative				
ORF1093	125133	125522	predied ferredoxin	AE001303	Chlamydia trachomatis	631	97
ORF1094	131888	131604	putative			-	
ORF1095	144164	144427	putative				
ORF1096	150698	150369	putative				

ORF	begin	stop	Homology	A	Species	Score	*i
ORF1097	164385	163948	NADH (Ubiquinone) Dehydrogenase	AE001300	Chlamydia trachomatis	755	100
ORF1098	165690	166115	hypothetical protein	AE001300	Chlamydia trachomatis	724	66
ORF1099	168742	168425	hypothetical protein	AE001300	Chlamydia trachomatis	356	96
ORF1100	170509	170793	hypothetical protein	AE001300	Chlamydia trachomatis	489	100
ORF1101	177145	177474	Accoa Carboxylase/Transferase Alpha	AE001299	Chlamydia trachomatis	518	6
ORF1102	188295	188023	hypothetical protein	AE001298	Chlamydia trachomatis	451	100
ORF1103	188791	188330	hypothetical protein	AE001298	Chlamydia trachomatis	733	97
ORF1104	190629	190336	putative				
ORF1105	197313	197083	putative				
ORF1106	210914	211384	putative				
ORF1107	235160	234852	Glutamate Aminomutase	AE001295	Chlamydia trachomatis	507	97
ORF1108	237227	236913	putative				
ORF1109	249733	249446	Oligopeptide Permease	AE001293	Chlamydia trachomatis	512	100
ORF1110	253493	253158	hypothetical protein	AE001293	Chlamydia trachomatis	318	63
ORF1111	253701	254789	hypothetical protein	AE001293	Chlamydia trachomatis	1860	66
ORF1112	271633	271932	hypothetical protein	AE001291	Chlamydia trachomatis	512	100
ORF1113	275666	276070	Disulfide bond Oxidoreductase	AE001291	Chlamydia trachomatis	, 002	66
ORF1114	277931	278218	putative				

ORF	pegin	stop	Homology	Ωī	Species	Score	% H
ORF1115	282741	282481	hypothetical protein	AE001290	Chlamydia trachomatis	422	66
ORF1116	293178	293489	Phospholipase D Endonuclease Superfamily	AE001289	Chlamydia trachomatis	433	95
ORF1117	303155	303469	putative				
ORF1118	309297	308965	hypothetical protein	AE001287	Chlamydia trachomatis	422	95
ORF1119	312219	312536	putative				
ORF1120	312853	312602	hypothetical protein	AE001287	Chlamydia trachomatis	338	66
ORF1121	313167	312772	hypothetical protein	AE001287	Chlamydia trachomatis	616	98
ORF1122	320224	320598	hypothetical protein	AE001286	Chlamydia trachomatis	628	98
ORF1123	340249	340503	Oligopeptidase	AE001285	Chlamydia trachomatis	444	100
ORF1124	352839	353324	hypothetical protein	AE001284	Chlamydia trachomatis	751	98
ORF1125	373475	373699	Phopholipase D Superfamily [leader (33) peptide}	AE001282	Chlamydia trachomatis	378	100
ORF1126	377316	377756	hypothetical protein	AE001282	Chlamydia trachomatis	764	66
ORF1127	379268	379657	hypothetical protein	AE001282	Chlamydia trachomatis	535	100
ORF1128	395098	394823	putative				
ORF1129	401594	401142	Flagellar Secretion Protein	AE001280	Chlamydia trachomatis	869	100
ORF1130	410045	410539	hypothetical protein	AE001279	Chlamydia trachomatis	767	100
ORF1131	411425	411658	Coproporphyrinogen III Oxidase	AE001279	Chlamydia trachomatis	399	66
ORF1132	414937	414416	putative				

007 007	610 100		1010 98														
Chlamydia trachomatis	dia trachomatis		dia trachomatis	1	1 1 1 1							dia trachomatis dia trachomatis dia trachomatis dia trachomatis dia trachomatis		dia trachomatis dia trachomatis dia trachomatis dia trachomatis dia trachomatis dia trachomatis dia trachomatis			
	78 Chlamydia		78 Chlamydia														
0000	AE0012/8	AE001278		AE001277	AE001277 AE001277	AE001277 AE001277	AE001277 AE001277	AE001277 AE001277	AE001277 AE001277 AE001361	AE001277 AE001361 AE001360							
Glycogen Hydrolase	(debranching) hypothetical protein		nypornericai procein		1 1-1	nypornetical protein hypothetical protein L31 Ribosomal Protein putative	nypornetical protein hypothetical protein L31 Ribosomal Protein putative	hypothetical protein hypothetical protein L31 Ribosomal Protein putative putative	hypothetical protein L31 Ribosomal Protein putative putative putative Putative Putative Putatine Protein I	ol er pr	pr br	protein Protein Protein	protein Protein Protein Protein Protein Protein Protein Protein	protein Protein	protein protein or Membra or Membra or Protea ter perme protein protein	protein protein or Response ter perme protein protein	protein protein ol Protein ter perme protein protein protein
423212 (debra	428183	429451 hypoth		442799 hypoth	һурс	hypo L31	hypo L31 puta	hypc Li31 puta puta	hypo List puta puta Puta Puta	hypc L31 puta puta puta Puta	hypo puta puta puta puta puta puta puta puta	hypo puta puta puta Puta Prot Memb	hypc puta	hypc L31 puta puta puta Prot Prot Puta Prot ABC	hypo puta puta puta puta Prot Low H H H ABC hypo	hypc L31 L31 puta puta puta Prot hypc hypc	hypo hypo hypo hypo hypo hypo
422889 45	427842 43	-	442557 44	_													
ORF1133	ODE1134	ORF1135	ORF1136		ORF1137	ORF1137 ORF1138	ORF1137 ORF1138 ORF1139	ORF1137 ORF1138 ORF1139	ORF1137 ORF1138 ORF1139 ORF1140	ORF1137 ORF1138 ORF1140 ORF1141 ORF1142	ORF1137 ORF1138 ORF1139 ORF1140 ORF1142 ORF1143	ORF1137 ORF1138 ORF1140 ORF1141 ORF1142 ORF1143	ORF1137 ORF1139 ORF1140 ORF1141 ORF1142 ORF1143 ORF1144	ORF1137 ORF1138 ORF1140 ORF1141 ORF1142 ORF1144 ORF1145	ORF1137 ORF1138 ORF1140 ORF1141 ORF1142 ORF1144 ORF1145 ORF1145	ORF1137 ORF1139 ORF1140 ORF1141 ORF1144 ORF1145 ORF1146 ORF1146 ORF1146	ORF1137 ORF1139 ORF1140 ORF1141 ORF1144 ORF1145 ORF1146 ORF1147 ORF1147

% H	53	100	66	97	100	98		66					66			98				98		96
Score	220	925	441	273	442	1176		434					324			864				606		661
Species	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis	Chlamydia trachomatis		Chlamydia trachomatis					Chlamydia trachomatis			Chlamydia trachomatis				Chlamydia trachomatis		Chlamydia trachomatis
e i	AE001353	AE001353	AE001353	AE001352	AE001351	AE001350		AE001349					AE001345			AE001343				AE001336		AE001335
Homology	Glycerol-3-P Acyltransferase	Insulinase family/Protease III	hypothetical protein	General Stress Protein	hypothetical protein	hypothetical protein	putative	hydrolase/phosphatase homolog	putative	putative	putative	putative	Phenolhydrolase/NADH ubiquinone oxidoreductase	putative	putative	hypothetical protein	putative	putative	putative	(Pseudouridine Synthase)	putative	hypothetical protein
stop	567232	570890	571332	575801	039065	262869	606626	607786	610391	633353	637482	649924	652562	655325	660810	677057	679253	732210	742383	758782	760521	770894
begin	566963	570351	571072	576025	590363	597868	688909	608031	610110	632703	637213	650517	652317	654753	661118	677596	679528	732536	742069	759318	760282	771313
ORF	ORF1151	ORF1152	ORF1153	ORF1154	ORF1155	ORF1156	ORF1157	ORF1158	ORF1159	ORF1160	ORF1161	ORF1162	ORF1163	ORF1164	ORF1165	ORF1166	ORF1167	ORF1168	ORF1169	ORF1170	ORF1171	ORF1172

ORF1173 772115 772408 hypothetical protein AE0013 ORF1174 788137 788457 putative AE0013 ORF1175 816302 816914 putative AE0013 ORF1176 867803 868054 putative AE0013 ORF1178 875386 875658 hypothetical protein AE0013 ORF1179 876445 876915 hypothetical protein AE0013 ORF1181 891859 891467 hypothetical protein AE0013 ORF1181 90253 902269 putative AE0013 ORF1184 908046 907783 putative AE0013 ORF1185 912313 912567 hypothetical protein AE0013 ORF1186 95451 946692 hypothetical protein AE0013 ORF1186 953193 952783 hypothetical protein AE0013 ORF1189 966199 966965 putative AE0013 ORF1190 970731 2-Component Sensor AE0013 <th>ID Species Score I%</th>	ID Species Score I%
788137 788457 putative 816302 815967 putative 846606 846914 putative 867803 868054 putative 875386 875658 hypothetical protein 876445 876915 hypothetical protein 891859 891467 hypothetical protein 891859 891467 putative 902553 902269 putative 902553 902269 putative 912313 912567 myristoyl GlcNac Deacetylase 935451 935741 putative 946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 968765 putative 971009 970731 2-Component Sensor 973119 973508 Phosphatase 973119 973508 Phosphoglycolate Phosphatase 966199 Phosphoglycolate Phosphatase 973119 973508 Phosphoglycolate Phosphatase 973119 973508 Phosphoglycolate Phosphatase 966199 Phosphoglycolate Phosphatase 973119 973508 Phosphoglycolate 973110 973508 Phosphoglycolate 973110 973508 Phosphoglycolate 973110 973508 Phosphoglycolate 973111 973111 973508 973111 973508 Phosphoglycolate 973111	AE001335 Chlamydia trachomatis 520 99
816302 815967 putative 846606 846914 putative 867803 868054 putative 875386 875658 hypothetical protein 884548 884312 putative 891859 891467 hypothetical protein 902553 902269 putative 908046 907783 putative 912313 912567 Myristoyl GlcNac Deacetylase 915451 935741 putative 946961 946692 hypothetical protein 966199 965873 hypothetical protein 966199 968765 putative 971009 970731 2-Component Sensor 971162 972404 putative 973119 973508 Phosphadatese	
8 46606 8 46914 putative 8 67803 868054 putative 8 75386 8 7558 hypothetical protein 8 84548 8 84312 putative 8 84548 8 844312 putative 900770 900417 putative 902553 902269 putative 912313 912567 Myristoyl GlcNac Deacetylase 915451 935741 putative 946961 946692 hypothetical protein 966199 965873 hypothetical protein 962298 968765 putative 971009 970731 2-Component Sensor 97162 972404 putative 973199 968765 putative	
867803 868054 putative 875386 875658 hypothetical protein 876445 876915 hypothetical protein 884548 884312 putative 891859 891467 hypothetical protein 900770 900417 putative 902553 902269 putative 912313 912567 Myristoyl GlcNac Deacetylase 946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 965873 hypothetical protein 96100 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphoglycolate Phosphatase	
## ## ## ## ## ## ## ## ## ## ## ## ##	
876445 876915 hypothetical protein 884548 884312 putative 891859 891467 hypothetical protein 900770 900417 putative 902553 902269 putative 908046 907783 putative 912313 912567 Myristoyl GlcNac Deacetylase 946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphaglycolate Phosphatase	AE001327 Chlamydia trachomatis 268 86
884548 884312 putative 891859 891467 hypothetical protein 900770 900417 putative 908046 907783 putative 912313 912567 Myristoyl GlcNac Deacetylase 912313 912567 Myristoyl GlcNac Deacetylase 946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphoglycolate Phosphatase	1 AE001327 Chlamydia trachomatis 747 99
891859 891467 hypothetical protein 900770 900417 putative 902553 902269 putative 912313 912567 Myristoyl GlcNac Deacetylase 935451 935741 putative 946961 946692 hypothetical protein 9613193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphoglycolate Phosphatase	
900770 900417 putative 902553 902269 putative 908046 907783 putative 912313 912567 Myristoyl GlcNac Deacetylase 935451 935741 putative 946961 946692 hypothetical protein 953193 955783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative Phosphatase	AE001326 Chlamydia trachomatis 551 95
902553 902269 putative 908046 907783 putative 912313 912567 Myristoyl GlcNac Deacetylase 935451 935741 putative 946961 946692 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphatase	
908046 907783 putative 912313 912567 Myristoyl GlcNac Deacetylase 935451 935741 putative 946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphatase	
912313 912567 Myristoyl GlcNac Deacetylase 935451 935741 putative 946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphatase	
935451 935741 putative 946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative Phosphatase	cetylase AE001324 Chlamydia trachomatis 195 97
946961 946692 hypothetical protein 953193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphoglycolate Phosphatase	
953193 952783 hypothetical protein 966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphaglycolate Phosphatase	AE001322 Chlamydia trachomatis 410 99
966199 965873 hypothetical protein 969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphoglycolate Phosphatase	AE001322 Chlamydia trachomatis 593 100
969298 968765 putative 971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphoglycolate Phosphatase	AE001321 Chlamydia trachomatís 542 98
971009 970731 2-Component Sensor 972162 972404 putative 973119 973508 Phosphoglycolate Phosphatase	
972162 972404 putative Phosphoglycolate Phosphatase	AE001320 Chlamydia trachomatis 467 97
973119 973508 Phosphoglycolate Phosphatase	
	sphatase AE001320 Chlamydia trachomatis 647, 98
ORF1194 998649 998404 putative	

ORF	begin	stop	Homology	ΩI	Species	Score I%	% 11%
ORF1195	1004280	1003882	hypothetical protein	AE001317	AE001317 Chlamydia trachomatis	571	66
ORF1196	1010200	1009532	hypothetical protein	AE001317	Chlamydia trachomatis	1132	66
ORF1197	1029174	1029482	putative				

TABLE 2

SEQ ID NO	begin	stop	preferred start
2	501	208	501
3	3276	505	3153
4	5068	3242	5062
5	6400	5126	6400
6	7977	6619	7977
7	8582	8082	8582
8	8995	8591	8995
9	9440	8979	9440
10	9828	10430	9828
11	10367	11254	10430
12	11245	11916	11245
13	12068	13324	12068
14	13532	14413	13538
15	14807	15019	14807
16	14932	15969	14977
17	15995	16501	16004
18	16467	16138	16377
19	18190	17417	18178
20	20521	18437	20518
21	22202	20814	22166
22	22602	22153	22509
23	22804	22478	22795
24	23183	22824	23180
25	23394	23110	23394
26	24569	23394	24569
27	26383	24641	26383
28	26640	27710	26640
29	28780	27725	28729
30	29957	28740	29957
31	30721	30032	30628
32	31281	30520	31254
33	31436	31780	31436

SEQ ID NO	begin	stop	preferred start
34	33356	31800	33344
35	33901	33314	33874
36	34116	35027	34116
37	34988	35359	35027
38	35167	35919	35377
39	35923	36996	36031
40	37810	37013	37765
41	38207	39085	38252
42	39151	39927	39157
43	39923	40756	39959
44	40760	42007	40772
45	42175	43116	42229
46	42999	43802	43128
47	44211	45227	44217
48	46072	45275	46066
49	46340	45975	46331
50	46895	46506	46865
51	47955	46882	47955
52	48585	48178	48558
53	50072	48630	50012
54	50710	50099	50692
55	52439	50925	52430
56	53484	52348	53478
57	54536	53466	54536
58	55086	54595	55104
59	56350	55031	56350
60	55659	56084	55722
61	56847	58235	56931
62	58423	59181	58423
63	59185	60195	59194
64	60188	61483	60191
65	61496	62353	61496
66	62500	63141	62518
67	63396	63983	63396

SEQ ID NO	begin	stop	preferred start
68	64628	64071	64580
69	64285	64656	64285
70	64944	64609	64938
71	65347	67269	65347
72	67656	68873	67815
73	68877	69233	68892
74	69212	69721	69323
75	69958	70455	69970
76	70701	71006	70725
77	73191	71086	73185
78	74900	73497	74891
79	75463	74876	75463
80	77124	75502	77124
81	77000	77299	77012
82	78095	77145	78095
83	79065	78154	79065
84	81971	79878	81965
85	82639	83271	82642
86	83792	84850	83921
87	84876	86921	84888
88	88650	87313	88383
89	87440	87805	87458
90	88400	88747	88409
91	88717	89265	88729
92	89355	89732	89355
93	89735	91447	89735
94	91749	91435	91749
95	92392	91745	92323
96	93138	92344	92874
97	94134	93361	93945
98	94637	94071	94577
99	98299	94628	98113
100	98715	98113	98715
101	100228	98741	100195

SEQ ID NO	begin	stop	preferred start
102	101347	100337	101323
103	102210	101323	102210
104	102485	102210	102479
105	104315	102726	104315
106	105075	104254	105075
107	105259	105894	105271
108	107429	108460	107486
109	108665	108955	108683
110	109459	109013	109456
111	110366	109704	110363
112	111330	112520	111330
113	112915	113463	112918
114	113566	113994	113566
115	114020	114604	114020
116	114720	115253	114807
117	115362	115676	115380
118	116022	119795	116040
119	119823	124010	119823
120	124065	124988	124065
121	124873	125106	124873
122	126261	125536	126243
123	126328	126930	126331
124	127138	127785	127147
125	127924	129714	127942
126	129720	131033	129720
127	131018	131629	131021
128	131834	133156	131852
129	133075	133584	133096
130	133625	133999	133628
131	133861	134508	133948
132	134638	137454	134638
133	137442	140276	137472
134	140733	140335	140727
135	141799	141077	141799

SEQ ID NO	begin	stop	preferred start
136	143240	141780	143240
137	143829	143128	143820
138	143923	144393	143923
139	144548	146326	144548
140	146413	147078	146425
141	147140	148075	147152
142	148115	148549	148115
143	148524	149027	148524
144	149000	149305	149033
145	149187	149708	149187
146	149712	150911	149769
147	152044	151004	151966
148	152664	151999	152592
149	152900	153352	152924
150	153389	153997	153425
151	155276	153984	155228
152	156544	155231	156544
153	156806	157525	156809
154	157489	158955	157534
155	159104	159961	159104
156	159916	161220	159916
157	161183	161593	161228
158	162354	161623	162354
159	163013	162363	163013
160	163941	162994	163941
161	165505	164474	165505
162	166686	166093	166686
163	168171	166729	168171
164	169249	168848	169189
165	169586	170431	169607
166	170780	171334	170783
167	171333	172376	171390
168	172309	172722	172309
169	173048	174496	173048

SEQ ID NO	begin	stop	preferred start
170	174399	174968	174399
171	175267	175710	175267
172	175714	177009	175735
173	177423	178115	177468
174	178084	180021	178084
175	180704	180048	180635
176	181398	180631	181398
177	182594	181398	182594
178	182895	183656	182895
179	183665	184786	183665
180	186007	184796	186007
181	186848	186000	186791
182	187270	186749	187240
183	187426	187809	187429
184	189481	188798	189442
185	189693	190352	189693
186	190235	190510	190280
187	190785	191786	190824
188	191790	192464	191811
189	192392	193183	192500
190	193254	194630	193263
191	195046	194690	195037
192	195184	197031	195193
193	197018	197635	197024
194	197762	198208	197669
195	198963	197668	198954
196	199957	198962	199945
197	200327	199941	200306
198	200685	200266	200598
199	200962	200585	200962
200	201169	202377	201184
201	203441	202380	203441
202	203998	203471	203989
203	206449	204059	206434

SEQ ID NO	begin	stop	preferred start
204	207425	206811	207410
205	207506	208528	207506
206	208545	209471	208545
207	209471	210214	209471
208	210586	210816	210586
209	211332	210883	211293
210	212978	211374	212972
211	214134	212875	214134
212	214710	214168	214701
213	215143	214754	215128
214	216705	215236	216705
215	217917	216892	217911
216	217088	217441	217202
217	218364	218702	218364
218	218695	219009	218785
219	219179	219748	219260
220	219891	220430	219912
221	220499	221074	220505
222	221137	221541	221176
223	221601	222092	221616
224	222472	223290	222487
225	223423	223818	223423
226	224278	225171	224278
227	225749	225174	225749
228	225334	225549	225328
229	226654	225749	226654
230	227299	226769	227170
231	227646	227161	227646
232	228457	227750	228439
233	230001	228607	229854
234	231074	230151	231062
235	231348	233006	231366
236	233059	233829	233059
237	233801	234265	233801

SEQ ID NO	begin	stop	preferred start
238	234282	234854	234288
239	236300	235227	236300
240	236314	238209	236314
241	238164	238769	238185
242	238769	240061	238769
243	242022	240313	242022
244	242846	241941	242846
245	244480	242798	244456
246	245897	244479	245891
247	246877	245924	246829
248	247731	246985	247725
249	248585	247743	248573
250	249420	248569	249411
251	250383	249766	250383
252	251186	250545	251174
253	252111	251095	252099
254	253088	252066	253088
255	255153	256718	255153
256	256762	257844	256774
257	257911	258690	257962
258	258780	259187	258840
259	259193	261604	259193
260	261622	264129	261622
261	264125	264742	264134
262	264741	265628	264759
263	266416	265631	266416
264	266938	266426	267946
265	267961	266942	267946
266	268320	268066	268299
267	268510	268205	268510
268	270116	268500	270116
269	270892	270095	270856
270	271191	271613	271224
271	272219	272932	272243

WO 99/28475 PCT/IB98/01939

SEQ ID NO	begin	stop	preferred start
272	272884	273588	273079
273	274816	273596	274807
274	274821	275666	274953
275	277689	276103	277689
276	278268	278816	278298
277	279771	279013	279870
278	280777	279767	280762
279	281603	281295	281576
280	282104	281787	282086
281	284335	282794	284320
282	284460	284795	284550
283	284817	285674	284844
284	285637	286137	285670
285	286357	286677	286399
286	286681	287898	286852
287	288127	289227	288358
288	289744	290679	289744
289	290828	291535	291206
290	291514	292230	291514
291	292326	293048	292350
292	293330	294853	293525
293	295684	295010	295684
294	296336	295692	296294
295	297238	296243	297199
296	297791	298735	297791
297	298905	300458	298920
298	302152	300527	302131
299	304917	302071	304872
300	306157	304973	306142
301	306494	306111	306461
302	306963	306436	306963
303	308773	306977	308758
304	309881	309276	309869
305	310720	309872	310711

SEQ ID NO	begin	stop	preferred start
306	311570	310716	311570
307	312451	311972	312439
308	313435	314364	313462
309	314340	314738	314409
310	315526	314741	315445
311	316507	315665	316507
312	317284	316529	317284
313	317592	317338	317592
314	318470	317499	318416
315	317599	317874	317599
316	318947	318477	318887
317	319342	320142	319342
318	320544	321497	320682
319	321485	321937	321497
320	321901	322362	321943
321	322301	323140	322325
322	323144	324913	323177
323	325621	324977	325621
324	326268	325621	326262
325	326469	327203	326469
326	327281	328150	327302
327	328605	328204	328602
328	329066	328734	329066
329	329663	329292	329648
330	330666	329608	330663
331	331161	330670	331161
332	331731	331177	331731
333	332404	331721	332404
334	332779	333021	332779
335	333005	333589	333149
336	334357	333806	334321
337	334089	334361	334089
338	335142	334729	335124
339	335195	335602	335234

SEQ ID NO	begin	stop	preferred start
340	335673	335194	335673
341	336334	335903	336229
342	337378	336338	337378
343	339947	337347	339947
344	340507	341847	340576
345	341783	342022	341786
346	342249	342470	342249
347	342597	343370	342597
348	343361	344032	343379
349	343956	344225	343962
350	344357	345142	344357
351	345934	345161	345934
352	347102	346080	347102
353	347113	347940	347119
354	350164	348146	350113
355	350423	351283	350426
356	352207	351314	352207
357	352727	352245	352703
358	353709	353305	353709
359	354218	353670	354215
360	354721	354140	354721
361	354966	356672	354966
362	356700	357377	356700
363	357326	358093	357500
364	358035	360743	358035
365	360753	361121	360753
366	361162	361884	361162
367	361826	362746	361826
368	363859	362816	363859
369	364116	365195	364116
370	365198	365587	365198
371	365479	367320	365614
372	367341	368603	367341
373	368644	369081	368644

SEQ ID NO	begin	stop	preferred start
374	369088	370251	369088
375	370769	371086	370769
376	371203	372816	371209
377	373119	373529	373152
378	373614	374204	373776
379	374736	374224	374703
380	376391	374703	376382
381	377062	376748	377038
382	377853	378737	377871
383	378626	379048	378710
384	379017	379403	379038
385	380009	379641	379967
386	380187	381470	380187
387	381473	382567	381473
388	382704	383702	382728
389	383945	383655	383921
390	385217	383949	385211
391	385507	385178	385507
392	386845	385706	386842
393	386127	386627	386232
394	387372	386872	387351
395	387823	387338	387823
396	388250	387816	388106
397	389169	388237	389169
398	389955	389173	390087
399	390988	389945	390922
400	391514	391810	391514
401	392410	393996	392413
402	394170	395354	394185
403	395309	395992	395354
404	396538	396059	396529
405	397507	396542	397498
406	398753	397401	398747
407	399688	398909	399667

SEQ ID NO	begin	stop	preferred start
408	400167	399778	400167
409	401224	400034	401209
410	401776	402021	401776
411	402126	403220	402132
412	403348	405180	403354
413	403788	403276	403785
414	405165	405920	405165
415	407049	405955	407049
416	409773	407056	409764
417	410532	411416	410532
418	411707	413410	411722
419	413433	412606	413334
420	413404	413952	413449
421	413841	415112	413991
422	414379	413978	414220
423	416664	415177	416646
424	417456	416740	417456
425	418053	417721	418044
426	418603	418031	418582
427	419531	418647	419531
428	420190	419672	420190
429	421171	420245	421171
430	421988	421518	421988
431	422486	423043	422492
432	423226	425079	423295
433	426054	425146	426021
434	426985	426245	426967
435	427248	427817	427248
436	429560	429886	429623
437	430360	429857	430360
438	430637	430323	430628
439	430933	431787	430966
440	431658	431987	431688
441	432232	434475	432238

SEQ ID NO	begin	stop	preferred start
442	436308	434620	436269
443	436574	436272	436571
444	437685	436567	437595
445	438262	437894	438256
446	439127	438285	439031
447	439339	438986	439339
448	439705	439358	439705
449	441042	439699	441042
450	441911	441042	441911
451	442593	441898	442584
452	444505	446388	444505
453	448068	446452	448029
454	449575	447932	449575
455	450546	451076	450576
456	451623	451144	451401
457	452593	451517	452575
458	453195	452632	453174
459	453567	454868	453567
460	455430	454972	455403
461	456047	455367	456047
462	457384	456047	457384
463	457659	458450	457659
464	458508	459632	458511
465	459839	461203	459839
466	461624	461196	461624
467	461887	462621	462151
468	463758	462895	463749
469	464048	464629	464063
470	464721	465848	464760
471	467420	466113	467414
472	468891	467419	468891
473	469280	468906	469226
474	469349	469675	469406
475	471226	469826	471160

SEQ ID NO	begin	stop	preferred start
476	471624	471106	471609
477	471954	473267	471954
478	473252	473695	473252
479	473982	474527	474051
480	475198	474602	475195
481	476527	475613	476509
482	478640	476517	478640
483	479084	478665	479078
484	479723	479088	479720
485	480012	479668	479898
486	481466	479895	481412
487	481732	481496	481732
488	481864	483429	481870
489	483402	484964	483402
490	484898	487864	484970
491	485725	485222	485593
492	488204	489247	488321
493	488571	488233	488562
494	489440	490456	489473
495	492765	490507	492690
496	492357	492893	492654
497	493744	492737	493723
498	493875	494675	493875
499	494573	494869	494609
500	494835	495365	494955
501	495174	494872	495174
502	495687	496634	495732
503	496295	497176	496523
504	497703	498515	498222
505	498280	499239	498301
506	499215	500732	499254
507	501710	500790	501710
508	502863	501808	502830
509	503675	502692	503645

SEQ ID NO	begin	stop	preferred star
510	505002	503722	505002
511	505739	506986	505739
512	506999	507439	507011
513	508404	507649	508302
514	508291	508590	508297
515	508915	508478	508915
516	509600	510691	509600
517	511039	511527	511147
518	511547	512185	511547
519	512382	513092	512385
520	514287	513055	514269
521	514789	515244	514792
522	514994	515269	515027
523	515553	515804	515553
524	515808	516422	515820
525	516476	517171	516605
526	517927	517400	517927
527	518096	518380	518114
528	518403	518822	518412
529	518923	519516	518923
530	519577	520497	519730
531	521986	520718	521971
532	522131	521886	522125
533	523495	522143	523483
534	524591	523623	524510
535	524652	525746	524685
536	525731	526078	525752
537	525939	526400	525999
538	526301	526735	526361
539	528323	526851	528284
540	528861	528292	528828
541	529723	529142	529645
542	530166	529624	530166
543	530543	530223	530543

SEQ ID NO	begin	stop	preferred start
544	531378	530737	531363
545	532370	533272	532370
546	533849	533244	533849
547	534672	533944	534615
548	535915	534878	535915
549	539153	535956	539114
550	539731	540519	539731
551	540523	540969	540526
552	540906	541805	541002
553	543255	541825	543222
554	544133	543222	544115
555	544565	544179	544532
556	544762	544487	544747
557	546423	544951	546423
558	547480	546584	547378
559	546789	547382	546900
560	547901	547476	547826
561	548634	547900	548634
562	548692	549459	548704
563	550385	549663	550376
564	551611	550421	551611
565	553041	551797	553041
566	554946	553096	554946
567	556300	554927	556300
568	556524	556904	556524
569	558126	557314	558105
570	557810	558235	557810
571	559215	558310	559215
572	561349	559196	561349
573	562931	561150	562898
574	564083	563121	564083
575	563593	563943	563644
576	565379	566953	565379
577	567079	567966	567274

SEQ ID NO	begin	stop	preferred start
578	568021	570399	568021
579	571269	572021	571284
580	572519	572755	572519
581	573519	572731	573393
582	572879	573427	573077
583	574160	573660	574160
584	574426	574184	574426
585	574781	574446	574781
586	575243	574923	575156
587	575458	575057	575458
588	575849	575469	575735
589	576545	578023	576545
590	578673	578017	578673
591	579012	582104	579012
592	582697	582206	582682
593	583122	582811	583095
594	583514	583182	583484
595	583869	583438	583803
596	584435	583827	584399
597	584967	584299	584967
598	585297	585016	585285
599	585240	586610	585300
600	586484	587758	586505
601	587786	589408	587786
602	589198	589578	589258
603	590061	589630	589971
604	590739	591272	590775
605	592406	592765	592406
606	593145	592849	593127
607	593900	593121	593894
608	594138	595637	594138
609	596122	595640	596053
610	596864	596154	596828
611	597731	597282	597689

SEQ ID NO	begin	stop	preferred start
612	598524	600809	598551
613	601876	600734	601864
614	603523	601910	603520
615	603794	603531	603794
616	604413	603757	604398
617	604549	605610	604549
618	606619	605582	606619
619	606843	607493	606867
620	609068	608031	608972
621	609652	609296	609652
622	611860	610109	611830
623	611812	612927	611815
624	613597	612938	613444
625	613952	613692	613952
626	614315	615244	614441
627	615396	615683	615396
628	617711	615864	617624
629	618313	617510	618361
630	619338	618361	619338
631	620416	619247	620401
632	619863	620261	619929
633	621184	620420	621154
634	621690	621154	621678
635	622399	621674	622399
636	623466	622414	623421
637	624178	623570	624106
638	624918	624073	624918
639	625346	626665	625367
640	626514	626900	626652
641	626954	627853	626984
642	627822	628124	627873
643	628715	628146	628715
644	628932	629801	628935
645	630406	629804	630298

SEQ ID NO	begin	stop	preferred start
646	630960	630298	630915
647	631799	630915	631799
648	637488	638084	637488
649	638036	640207	638111
650	640221	643472	640236
651	640627	640220	640627
652	643485	644495	643488
653	644471	645430	644471
654	645394	645840	645538
655	645840	647111	645840
656	649676	647109	649616
657	649970	650344	649970
658	650418	651722	650433
659	651686	652171	651770
660	652516	652908	652516
661	652799	653593	652892
662	659884	661851	660136
663	661740	662282	661851
664	662286	663074	662289
665	662951	663730	663074
666	664212	663745	664194
667	665619	664255	665619
668	666083	665727	666056
669	666423	665782	666390
670	666831	668117	667047
671	668121	668375	668139
672	668470	668174	668404
673	669533	668616	669485
674	669892	669485	669892
675	670780	669998	670765
676	671241	670732	671196
677	671182	672447	671260
678	672692	673231	672698
679	673204	674562	673204

SEQ ID NO	begin	stop	preferred start
680	674612	675232	674612
681	675327	676463	675327
682	677027	676476	677027
683	678422	677700	678422
684	678717	679508	678708
685	679342	680502	679342
686	680579	681280	680654
687	681539	682558	681557
688	682554	683087	682578
689	683164	684465	683164
690	684774	684418	684639
691	684839	686203	684839
692	686197	687204	686203
693	687341	688360	687341
694	688432	688193	688426
695	689616	688432	689601
696	689960	689631	689939
697	690487	689846	690445
698	690717	690463	690717
699	691871	690672	691856
700	693837	692041	693837
701	694934	693837	694934
702	697263	694942	697230
703	698084	697170	697958
704	698392	697979	698380
705	698792	700117	698792
706	700269	700895	700269
707	700912	702165	700990
708	702183	703412	702183
709	703522	705000	703531
710	705011	705604	705062
711	706159	705704	706093
712	706521	706138	706488
713	708103	706496	707932

SEQ ID NO	begin	stop	preferred star
714	708398	708078	708392
715	708610	708248	708610
716	710278	708872	710203
717	711164	710262	711164
718	711432	712763	711432
719	712767	713438	712773
720	714232	713651	714217
721	714632	714120	714617
722	715592	714834	715739
723	715854	715558	715854
724	716937	715921	716886
725	718357	717149	718357
726	718500	718862	718590
727	719797	718499	719776
728	720273	719782	720147
729	720452	720144	720452
730	720613	721575	720613
731	721559	722356	721571
732	723248	722397	723239
733	724598	723378	724580
734	725763	724576	725760
735	726519	725767	726519
736	726819	726538	726801
737	727493	726753	727466
738	727984	727469	727984
739	728778	728329	728718
740	729346	728759	729334
741	732639	729442	732639
742	733246	734427	733246
743	734814	735659	734814
744	735644	736504	735644
745	736520	737254	736520
746	737254	737787	737254
747	737942	738679	738122

SEQ ID NO	begin	stop	preferred start
748	738838	739740	738862
749	742057	740060	741982
750	742869	742045	742824
751	743378	742824	743348
752	744298	743306	744292
753	744714	744430	744660
754	744985	744611	744931
755	745557	744958	745548
756	746412	745561	746409
757	746772	746416	746697
758	748269	746944	748269
759	748966	748274	748954
760	749426	748965	749411
761	749702	749433	749681
762	750029	749721	750020
763	752307	750007	752307
764	752913	752503	752901
765	754659	753616	754659
766	755000	756814	755000
767	756796	758301	756832
768	758691	758446	758688
769	759787	759338	759787
770	760242	759871	760188
771	760538	760188	760529
772	760966	761772	760966
773	761759	762142	761759
774	762267	762983	762267
775	764465	763335	764312
776	764857	764438	764821
777	766068	764821	765972
778	766643	766065	766643
779	768091	766934	768091
780	768785	768252	768785
781	770092	768791	770062

SEQ ID NO	begin	stop	preferred start
782	770138	770470	770150
783	770661	770185	770631
784	770924	770634	770894
785	772010	771330	772010
786	772390	773391	772390
787	774221	773427	774215
788	776035	774191	776035
789	776663	777706	776894
790	777195	776953	777177
791	779222	777732	779180
792	779321	781552	779360
793	781297	782442	781351
794	782447	785524	782447
795	785532	786002	785697
796	786580	785546	786580
797	787741	786611	787729
798	787620	788021	787782
799	790124	787920	790064
800	790160	790609	790178
801	790634	792016	790634
802	793084	792059	793084
803	793343	794056	793370
804	794046	794957	794079
805	795401	795144	795395
806	795575	796255	795575
807	796278	797015	796311
808	796979	797365	796979
809	797260	797856	797395
810	797772	798086	797805
811	798426	797935	798393
812	798925	798416	798916
813	799301	799927	799301
814	800892	800029	800892
815	801062	802129	801062

SEQ ID NO	begin	stop	preferred start
816	802023	802673	802041
817	802851	803246	802920
818	803105	804220	803111
819	804307	805356	804331
820	805290	806282	805356
821	806453	808081	806498
822	808026	809009	808098
823	810461	809079	810437
824	811605	810328	811590
825	811725	812342	811824
826	812329	813522	812398
827	813455	813772	813455
828	813732	814334	813780
829	815213	814314	815207
830	814878	814396	814975
831	815733	815428	815733
832	816116	817456	816170
833	817608	819320	817608
834	819324	819713	819342
835	819704	820402	819713
836	820375	821061	820453
837	821043	821537	821043
838	821646	822239	821667
839	822182	822931	822221
840	824355	823045	824352
841	825894	824359	825891
842	826322	825879	826322
843	826340	827026	826340
844	827014	827250	827014
845	827856	827230	827856
846	828007	829275	828025
847	829355	830953	829358
848	831119	831748	831140
849	832152	831751	832140

SEQ ID NO	begin	stop	preferred start
850	832744	832214	832666
851	833446	832805	833446
852	833802	833368	833742
853	834679	833879	834661
854	835452	834661	835365
855	835778	835371	835775
856	836482	835775	836470
857	836602	837264	836617
858	837209	838699	837209
859	838760	839575	838760
860	839942	840583	839951
861	840445	841713	840451
862	841659	842459	841686
863	842523	843068	842541
864	843495	843031	843447
865	843239	846196	843335
866	844137	843802	844077
867	848043	846217	848022
868	850123	848150	850099
869	851645	850230	851504
870 ·	853696	851669	853672
871	854836	853700	854809
872	855525	854920	855468
873	856240	855437	856240
874	857183	856233	857006
875	859439	857451	859430
876	859946	859587	859916
877	859642	860640	859660
878	861599	860724	861599
879	862053	861580	862038
880	863540	862098	863531
881	863930	863571	863927
882	864697	863996	864688
883	864923	866248	864923

SEQ ID NO	begin	stop	preferred start
884	866303	866605	866336
885	866665	867732	866665
886	867810	869090	867864
887	869094	869357	869094
888	869270	871372	869336
889	871299	872582	871359
890	872429	872860	872555
891	872773	873915	872773
892	873812	873360	873668
893	874028	874438	874067
894	874778	875386	874796
895	875774	876382	875843
896	877872	877000	877866
897	878172	877876	878157
898	879098	878172	879098
899	878883	879161	878886
900	879842	879105	879809
901	880885	880052	880885
902	881863	880889	881863
903	882904	881948	882901
904	883794	882901	883761
905	884296	883661	884296
906	884996	884508	884984
907	888777	885166	888771
908	890172	888940	890172
909	891164	890325	891146
910	891463	891116	891427
911	893278	891968	893278
912	893356	893808	893386
913	893909	893643	893894
914	894276	893821	894276
915	894778	894248	894760
916	895892	895050	895874
917	895951	896829	895963

SEQ ID NO	begin	stop	preferred start
918	900783	897064	900774
919	902032	900791	902158
920	902659	903876	902659
921	903731	903471	903731
922	903860	905605	903860
923	905725	906474	905725
924	906493	906945	906493
925	907306	907001	907306
926	908101	908742	908131
927	908721	909194	908724
928	909198	909584	909201
929	909583	909951	909670
930	910081	910569	910090
931	910615	910944	910636
932	910948	912261	910951
933	912399	912629	912399
934	912595	913218	912595
935	913203	913676	913218
936	913691	914485	913691
937	914516	915136	914522
938	915144	915467	915162
939	915629	916633	915629
940	916051	916539	916159
941	916965	917627	916965
942	917612	918304	917612
943	918323	918655	918323
944	918682	919533	918682
945	919542	919829	919542
946	919723	920157	919723
947	920184	920840	920184
948	920866	921294	920866
949	921272	921514	921272
950	921510	921758	921510
951	921778	922143	921778

PCT/IB98/01939

SEQ ID NO	begin	stop	preferred start
986	949849	950676	949888
987	950680	951330	950701
988	951281	951643	951290
989	951788	952798	951803
990	953581	954264	953602
991	954426	955157	954429
992	955754	957940	955766
993	957837	959312	957867
994	959299	961050	959317
995	961562	961053	961562
996	962575	961487	962545
997	961979	961584	961979
998	964914	962545	964914
999	964941	965708	964956
1000	967023	966193	966984
1001	967444	968061	967459
1002	968903	968064	968792
1003	970685	969528	970685
1004	971806	971024	971785
1005	973053	972388	973026
1006	974546	973746	974546
1007	975223	974558	975214
1008	976193	975207	976193
1009	976520	976254	976511
1010	976588	976899	976588
1011	976886	977635	976934
1012	977661	977933	977682
1013	977918	978433	977933
1014	978619	978984	978619
1015	978933	979331	978987
1016	981197	979389	981197
1017	979711	980112	979753
1018	982116	981148	982107
1019	982321	983598	982321

SEQ ID NO	begin	stop	preferred start
1020	984488	983862	984296
1021	985381	984371	985381
1022	986103	985399	986046
1023	986693	986046	986693
1024	987607	986693	987607
1025	988119	987616	987942
1026	988253	987936	988247
1027	988831	989163	988834
1028	989693	993442	989693
1029	993408	993785	993408
1030	993835	993416	993754
1031	993882	994262	993906
1032	994226	995656	994259
1033	996036	996611	996036
1034	996885	998267	996885
1035	998962	999225	998962
1036	999375	1001033	999393
1037	1001211	1001516	1001214
1038	1001392	1001664	1001443
1039	1003721	1001823	1003721
1040	1004459	1004845	1004459
1041	1004990	1005382	1004990
1042	1005391	1007496	1005391
1043	1007486	1007821	1007453
1044	1007802	1008698	1007841
1045	1009426	1009121	1009426
1046	1010534	1012054	1010534
1047	1012397	1011942	1012241
1048	1012042	1012635	1012057
1049	1012593	1012862	1012593
1050	1012811	1013440	1012829
1051	1013456	1014055	1013468
1052	1013977	1014489	1013977
1053	1015224	1014529	1015206

SEQ ID NO	begin	stop	preferred start
1054	1016002	1015145	1015963
1055	1017120	1015939	1017120
1056	1017766	1017245	1017658
1057	1018911	1017916	1018893
1058	1019191	1018580	1019110
1059	1020199	1019831	1020196
1060	1021007	1020114	1020992
1061	1021569	1021075	1021557
1062	1022411	1022097	1022402
1063	1023344	1023667	1023344
1064	1023701	1023949	1023701
1065	1023976	1024776	1023976
1066	1024704	1025045	1024704
1067	1025881	1024967	1025845
1068	1026546	1025839	1026546
1069	1027379	1026546	1027373
1070	1030604	1027929	1030328
1071	1033252	1030508	1033249
1072	1031733	1032086	1031823
1073	1037037	1033456	1037016 .
1074	1035674	1035910	1035674
1075	1036175	1036507	1036268
1076	68(comp)	1036967	38
1077	16591	16989	16597
1078	31779	31408	.31764
1079	56502	56834	56520
1080	56686	56913	56686
1081	64748	65074	64790
1082	73482	73195	73482
1083	78482	78736	78506
1084	79803	79411	79773
1085	82333	81959	82333
1086	87313	86999	87523
1087	109929	109456	109716

SEQ ID NO	begin	stop	preferred start
1088	111599	111351	111599
1089	112069	111734	111988
1090	112666	112911	112666
1091	114017	113715	113978
1092	120757	120464	120757
1093	125133	125522	125133
1094	131888	131604	131837
1095	144164	144427	144191
1096	150698	150369	150635
1097	164385	163948	164385
1098	165690	166115	165408
1099	168742	168425	168742
1100	170509	170793	170509
1101	177145	177474	177145
1102	188295	188023	188295
1103	188791	188330	188791
1104	190629	190336	190626
1105	197313	197083	197307
1106	210914	211384	210956
1107	235160	234852	235160
1108	237227	236913	237188
1109	249733	249446	249904
1110	253493	253158	253493
1111	253701	254789	253701
1112	271633	271932	271633
1113	275666	276070	275666
1114	277931	278218	277976
1115	282741	282481	282738
1116	293178	293489	293181
1117	303155	303469	303185
1118	309297	308965	309297
1119	312219	312536	312246
1120	312853	312602	312844
1121	313167	312772	313167

SEQ ID NO	begin	stop	preferred start
1122	320224	320598	320224
1123	340249	340503	340249
1124	352839	353324	352839
1125	373475	373699	373475
1126	377316	377756	377316
1127	379268	379657	379268
1128	395098	394823	395077
1129	401594	401142	401594
1130	410045	410539	410045
1131	411425	411658	411425
1132	414937	414416	414937
1133	422889	423212	422964
1134	427842	428183	427842
1135	428732	429451	428732
1136	442557	442799	442524
1137	443628	444041	443628
1138	443678	443166	443678
1139	445901	446155	445901
1140	467981	468262	468023
1141	471869	472108	471869
1142	488032	488337	488044
1143	497179	497694	497101
1144	500474	500202	500471
1145	508968	509561	508968
1146	510845	511264	510845
1147	526525	526848	526525
1148	531318	531863	531444
1149	556826	557224	556826
1150	564971	564537	564971
1151	566963	567232	566963
1152	570351	570890	570351
1153	571072	571332	571072
1154	576025	575801	576025
1155	590363	590650	590363

SEQ ID NO	begin	Stop	preferred start
1156	597868	598593	597868
1157	606889	606626	606889
1158	608031	607786	608031
1159	610110	610391	610143
1160	632703	633353	632703
1161	637213	637482	637255
1162	650517	649924	650517
1163	652317	652562	652317
1164	654753	655325	654753
1165	661118	660810	661118
1166	677596	677057	677578
1167	679528	679253	679477
1168	732536	732210	732536
1169	742069	742383	742069
1170	759318	758782	759318
1171	760282	760521	760282
1172	771313	770894	771391
1173	772115	772408	772115
1174	788137	788457	788137
1175	816302	815967	816302
1176	846606	846914	846612
1177	867803	868054	867806
1178	875386	875658	875395
1179	876445	876915	876445
1180	884548	884312	884548
1181	891859	891467	891859
1182	900770	900417	900728
1183	902553	902269	902529
1184	908046	907783	908007
1185	912313	912567	912313
1186	935451	935741	935451
1187	946961	946692	946940
1188	953193	952783	953145
1189	966199	965873	966184

SEQ ID NO	begin	stop	preferred start
1190	969298	968765	969298
1191	971009	970731	971009
1192	972162	972404	972165
1193	973119	973508	973119
1194	998649	998404	998625
1195	1004280	1003882	1004280
1196	1010200	1009532	1010200
1197	1029174	1029482	1029180

TABLE 4

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
2	1199	1198	3591	3590
3	1201	1200	3593	3592
4	1203	1202	3595	3594
5	1205	1204	3597	3596
6	1207	1206	3599	3598
7	1209	1208	3601	3600
8	1211	1210	3603	3602
9	1213	1212	3605	3604
10	1215	1214	3607	3606
11	1217	1216	3609	3608
12	1219	1218	3611	3610
13	1221	1220	3613	3612
14	1223	1222	3615	3614
15	1225	1224	3617	3616
16	1227	1226	3619	3618
17	1229	1228	3621	3620
18	1231	1230	3623	3622
19	1233	1232	3625	3624
20	1235	1234	3627	3626
21	1237	1236	3629	3628
22	1239	1238	3631	3630
23	1241	1240	3633	3632
24	1243	1242	3635	3634
25	1245	1244	3637	3636
26	1247	1246	3639	3638
27	1249	1248	3641	3640
28	1251	1250	3643	3642
29	1253	1252	3645	3644
30	1255	1254	3647	3646
31	1257	1256	3649	3648
32	1259	1258	3651	3650
33	1261	1260	3653	3652

WO 99/28475 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
34	1263	1262	3655	3654
35	1265	1264	3657	3656
36	1267	1266	3659	3658
37	1269	1268	3661	3660
38	1271	1270	3663	3662
39	1273	1272	3665	3664
40	1275	1274	3667	3666
41	1277	1276	3669	3668
42	1279	1278	3671	3670
43	1281	1280	3673	3672
44	1283	1282	3675	3674
45	1285	1284	3677	3676
46	1287	1286	3679	3678
47	1289	1288	3681	3680
48	1291	1290	3683	3682
49	1293	1292	3685	3684
50	1295	1294	3687	3686
51	1297	1296	3689	3688
52	1299	1298	3691	3690
53	1301	1300	3693	3692
54	1303	1302	3695	3694
55	1305	1304	3697	3696
56	1307	1306	3699	3698
57	1309	1308	3701	3700
58	1311	1310	3703	3702
59	1313	1312	3705	3704
60	1315	1314	3707	3706
61	1317	1316	3709	3708
62	1319	1318	3711	3710
63	1321	1320	3713	3712
64	1323	1322	3715	3714
65	1325	1324	3717	3716
66	1327	1326	3719	3718
67	1329	1328	3721	3720

194					
ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp	
68	1331	1330	3723	3722	
69	1333	1332	3725	3724	
70	1335	1334	3727	3726	
71	1337	1336	3729	3728	
72	1339	1338	3731	3730	
73	1341	1340	3733	3732	
74	1343	1342	3735	3734	
75	1345	1344	3737	3736	
76	1347	1346	3739	3738	
77	1349	1348	3741	3740	
78	1351	1350	3743	3742	
79	1353	1352	3745	3744	
80	1355	1354	3747	3746	
81	1357	1356	3749	3748	
82	1359	1358	3751	3750	
83	1361	1360	3753	3752	
84	1363	1362	3755	3754	
85	1365	1364	3757	3756	
86	1367	1366	3759	3758	
87	1369	1368	3761	3760	
88	1371	1370	3763	3762	
89	1373	1372	3765	3764	
90	1375	1374	3767	3766	
91	1377	1376	3769	3768	
92	1379	1378	3771	3770	
93	1381	1380	3773	3772	
94	1383	1382	3775	3774	
95	1385	1384	3777	3776	
96	1387	1386	3779	3778	
97	1389	1388	3781	3780	
98	1391	1390	3783	3782	
99	1393	1392	3785	3784	
100	1395	1394	3787	3786	
101	1397	1396	3789	3788	

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
102	1399	1398	3791	3790
103	1401	1400	3793	3792
104	1403	1402	3795	3794
105	1405	1404	3797	3796
106	1407	1406	3799	3798
107	1409	1408	3801	3800
108	1411	1410	3803	3802
109	1413	1412	3805	3804
110	1415	1414	3807	3806
111	1417	1416	3809	3808
112	1419	1418	3811	3810
113	1421	1420	3813	3812
114	1423	1422	3815	3814
115	1425	1424	3817	3816
116	1427	1426	3819	3818
117	1429	1428	3821	3820
118	1431	1430	3823	3822
119	1433	1432	3825	3824
120	1435	1434	3827	3826
121	1437	1436	3829	3828
122	1439	1438	3831	3830
123	1441	1440	3833	3832
124	1443	1442	3835	3834
125	1445	1444	3837	3836
126	1447	1446	3839	3838
127	1449	1448	3841	3840
128	1451	1450	3843	3842
129	1453	1452	3845	3844
130	1455	1454	3847	3846
131	1457	1456	3849	3848
132	1459	1458	3851	3850
133	1461	1460	3853	3852
134	1463	1462	3855	3854
135	1465	1464	3857	3856

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
136	1467	1466	3859	3858
137	1469	1468	3861	3860
138	1471	1470	3863	3862
139	1473	1472	3865	3864
140	1475	1474	3867	3866
141	1477	1476	3869	3868
142	1479	1478	3871	3870
143	1481	1480	3873	3872
144	1483	1482	3875	3874
145	1485	1484	3877	3876
146	1487	1486	3879	3878
147	1489	1488	3881	3880
148	1491	1490	3883	3882
149	1493	1492	3885	3884
150	1495	1494	3887	3886
151	1497	1496	3889	3888
152	1499	1498	3891	3890
153	1501	1500	3893	3892
154	1503	1502	3895	3894
155	1505	1504	3897	3896
156	1507	1506	3899	3898
157	1509	1508	3901	3900
158	1511	1510	3903	3902
159	1513	1512	3905	3904
160	1515	1514	3907	3906
161	1517	1516	3909	3908
162	1519	1518	3911	3910
163	1521	1520	3913	3912
164	1523	1522	3915	3914
165	1525	1524	3917	3916
166	1527	1526	3919	3918
167	1529	1528	3921	3920
168	1531	1530	3923	3922
169	1533	1532	3925	3924

WO 99/28475 197 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
170	1535	1534	3927	3926
171	1537	1536	3929	3928
172	1539	1538	3931	3930
173	1541	1540	3933	3932
174	1543	1542	3935	3934
175	1545	1544	3937	3936
176	1547	1546	3939	3938
177	1549	1548	3941	3940
178	1551	1550	3943	3942
179	1553	1552	3945	3944
180	1555	1554	3947	3946
181	1557	1556	3949	3948
182	1559	1558	3951	3950
183	1561	1560	3953	3952
184	1563	1562	3955	3954
185	1565	1564	3957	3956
186	1567	1566	3959	3958
187	1569	1568	3961	3960
188	1571	1570	3963	3962
189	1573	1572	3965	3964
190	1575	1574	3967	3966
191	1577	1576	3969	3968
192	1579	1578	3971	3970
193	1581	1580	3973	3972
194	1583	1582	3975	3974
195	1585	1584	3977	3976
196	1587	1586	3979	3978
197	1589	1588	3981	3980
198	1591	1590	3983	3982
199	1593	1592	3985	3984
200	1595	1594	3987	3986
201	1597	1596	3989	3988
202	1599	1598	3991	3990
203	1601	1600	3993	3992

4	~
7	ux

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
204	1603	1602	3995	3994
205	1605	1604	3997	3996
206	1607	1606	3999	3998
207	1609	1608	4001	4000
208	1611	1610	4003	4002
209	1613	1612	4005	4004
210	1615	1614	4007	4006
211	1617	1616	4009	4008
212	1619	1618	4011	4010
213	1621	1620	4013	4012
214	1623	1622	4015	4014
215	1625	1624	4017	4016
216	1627	1626	4019	4018
217	1629	1628	4021	4020
218	1631	1630	4023	4022
219	1633	1632	4025	4024
220	1635	1634	4027	4026
221	1637	1636	4029	4028
222	1639	1638	4031	4030
223	1641	1640	4033	4032
224	1643	1642	4035	4034
225	1645	1644	4037	4036
226	1647	1646	4039	4038
227	1649	1648	4041	4040
228	1651	1650	4043	4042
229	1653	1652	4045	4044
230	1655	1654	4047	4046
231	1657	1656	4049	4048
232	1659	1658	4051	4050
233	1661	1660	4053	4052
234	1663	1662	4055	4054
235	1665	1664	4057	4056
236	1667	1666	4059	4058
237	1669	1668	4061	4060

WO 99/28475 199 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
238	1671	1670	4063	4062
239	1673	1672	4065	4064
240	1675	1674	4067	4066
241	1677	1676	4069	4068
242	1679	1678	4071	4070
243	1681	1680	4073	4072
244	1683	1682	4075	4074
245	1685	1684	4077	4076
246	1687	1686	4079	4078
247	1689	1688	4081	4080
248	1691	1690	4083	4082
249	1693	1692	4085	4084
250	1695	1694	4087	4086
251	1697	1696	4089	4088
252	1699	1698	4091	4090
253	1701	1700	4093	4092
254	1703	1702	4095	4094
255	1705	1704	4097	4096
256	1707	1706	4099	4098
257	1709	1708	4101	4100
258	1711	1710	4103	4102
259	1713	1712	4105	4104
260	1715	1714	4107	4106
261	1717	1716	4109	4108
262	1719	1718	4111	4110
263	1721	1720	4113	4112
264	1723	1722	4115	4114
265	1725	1724	4117	4116
266	1727	1726	4119	4118
267	1729	1728	4121	4120
268	1731	1730	4123	4122
269	1733	1732	4125	4124
270	1735	1734	4127	4126
271	1737	1736	4129	4128

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
272	1739	1738	4131	4130
273	1741	1740	4133	4132
274	1743	1742	4135	4134
275	1745	1744	4137	4136
276	1747	1746	4139	4138
277	1749	1748	4141	4140
278	1751	1750	4143	4142
279	1753	1752	4145	4144
280	1755	1754	4147	4146
281	1757	1756	4149	4148
282	1759	1758	4151	4150
283	1761	1760	4153	4152
284	1763	1762	4155	4154
285	1765	1764	4157	4156
286	1767	1766	4159	4158
287	1769	1768	4161	4160
288	1771	1770	4163	4162
289	1773	1772	4165	4164
290	1775	1774	4167	4166
291	1777	1776	4169	4168
292	1779	1778	4171	4170
293	1781	1780	4173	4172
294	1783	1782	4175	4174
295	1785	1784	4177	4176
296	1787	1786	4179	4178
297	1789	1788	4181	4180
298	1791	1790	4183	4182
299	1793	1792	4185	4184
300	1795	1794	4187	4186
301	1797	1796	4189	4188
302	1799	1798	4191	4190
303	1801	1800	4193	4192
304	1803	1802	4195	4194
305	1805	1804	4197	4196

WO 99/28475 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFaligasBd	ORFoligosBp
306	1807	1806	4199	4198
307	1809	1808	4201	4200
308	1811	1810	4203	4202
309	1813	1812	4205	4204
310	1815	1814	4207	4206
311	1817	1816	4209	4208
. 312	1819	1818	4211	4210
313	1821	1820	4213	4212
314	1823	1822	4215	4214
315	1825	1824	4217	4216
316	1827	1826	4219	4218
317	1829	1828	4221	4220
318	1831	1830	4223	4222
319	1833	1832	4225	4224
320	1835	1834	4227	4226
321	1837	1836	4229	4228
322	1839	1838	4231	4230
323	1841	1840	4233	4232
324	1843	1842	4235	4234
325	1845	1844	4237	4236
326	.1847	1846	4239	4238
327	1849	1848	4241	4240
328	1851	1850	4243	4242
329	1853	1852	4245	4244
330	1855	1854	4247	4246
331	1857	1856	4249	4248
332	1859	1858	4251	4250
333	1861	1860	4253	4252
334	1863	1862	4255	4254
335	1865	1864	4257	4256
336	1867	1866	4259	4258
337	1869	1868	4261	4260
338	1871	1870	4263	4262
339	1873	1872	4265	4264

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligôsBd	ORFoligosBp
340	1875	1874	4267	4266
341	1877	1876	4269	4268
342	1879	1878	4271	4270
343	1881	1880	4273	4272
344	1883	1882	4275	4274
345	1885	1884	4277	4276
346	1887	1886	4279	4278
347	1889	1888	4281	4280
348	1891	1890	4283	4282
349	1893	1892	4285	4284
350	1895	1894	4287	4286
351	1897	1896	4289	4288
352	1899	1898	4291	4290
353	1901	1900	4293	4292
354	1903	1902	4295	4294
355	1905	1904	4297	4296
356	1907	1906	4299	4298
357	1909	1908	4301	4300
358	1911	1910	4303	4302
359	1913	1912	4305	4304
360	1915	1914	4307	4306
361	1917	1916	4309	4308
362	1919	1918	4311	4310
363	1921	1920	4313	4312
364	1923	1922	4315	4314
365	1925	1924	4317	4316
366	1927	1926	4319	4318
367	1929	1928	4321	4320
368	1931	1930	4323	4322
369	1933	1932	4325	4324
370	1935	1934	4327	4326
371	1937	1936	4329	4328
372	1939	1938	4331	4330
373	1941	1940	4333	4332

. WO 99/28475 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
374	1943	1942	4335	4334
375	1945	1944	4337	4336
376	1947	1946	4339	4338
377	1949	1948	4341	4340
378	1951	1950	4343	4342
379	1953	1952	4345	4344
380	1955	1954	4347	4346
381	1957	1956	4349	4348
382	1959	1958	4351	4350
383	1961	1960	4353	4352
384	1963	1962	4355	4354
385	1965	1964	4357	4356
386	1967	1966	4359	4358
387	1969	1968	4361	4360
388	1971	1970	4363	4362
389	1973	1972	4365	4364
390	1975	1974	4367	4366
391	1977	1976	4369	4368
392	1979	1978	4371	4370
393	1981	1980	4373	4372
394	1983	1982	4375	4374
395	1985	1984	4377	4376
396	1987	1986	4379	4378
397	1989	1988	4381	4380
398	1991	1990	4383	4382
399	1993	1992	4385	4384
400	1995	1994	4387	4386
401	1997	1996	4389	4388
402	1999	1998	4391	4390
403	2001	2000	4393	4392
404	2003	2002	4395	4394
405	2005	2004	4397	4396
406	2007	2006	4399	4398
407	2009	2008	4401	4400

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
408	2011	2010	4403	4402
409	2013	2012	4405	4404
410	2015	2014	4407	4406
411	2017	2016	4409	4408
412	2019	2018	4411	4410
413	2021	2020	4413	4412
414	2023	2022	4415	4414
415	2025	2024	4417	4416
416	2027	2026	4419	4418
417	2029	2028	4421	4420
418	2031	2030	4423	4422
419	2033	2032	4425	4424
420	2035	2034	4427	4426
421	2037	2036	4429	4428
422	2039	2038	4431	4430
423	2041	2040	4433	4432
424	2043	2042	4435	4434
425	2045	2044	4437	4436
426	2047	2046	4439	4438
427	2049	2048	4441	4440
428	2051	2050	4443	4442
429	2053	2052	4445	4444
430	2055	2054	4447	4446
431	2057	2056	4449	4448
432	2059	2058	4451	4450
433	2061	2060	4453	4452
434	2063	2062	4455	4454
435	2065	2064 .	4457	4456
436	2067	2066	4459	4458
437	2069	2068	4461	4460
438	2071	2070	4463	4462
439	2073	2072	4465	4464
440	2075	2074	4467	4466
441	2077	2076	4469	4468

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
442	2079	2078	4471	4470
443	2081	2080	4473	4472
444	2083	2082	4475	4474
445	2085	2084	4477	4476
446	2087	2086	4479	4478
447	2089	2088	4481	4480
448	2091	2090	4483	4482
449	2093	2092	4485	4484
450	2095	2094	4487	4486
451	2097	2096	4489	4488
452	2099	2098	4491	4490
453	2101	2100	4493	4492
454	2103	2102	4495	4494
455	2105	2104	4497	4496
456	2107	2106	4499	4498
457	2109	2108	4501	4500
458	2111	2110	4503	4502
459	2113	2112	4505	4504
460	2115	2114	4507	4506
461	2117	2116	4509	4508
462	2119	2118	4511	4510
463	2121	2120	4513	4512
464	2123	2122	4515	4514
465	2125	2124	4517	4516
466	2127	2126	4519	4518
467	2129	2128	4521	4520
468	2131	2130	4523	4522
469	2133	2132	4525	4524
470	2135	2134	4527	4526
471	2137	2136	4529	4528
472	2139	2138	4531	4530
473	2141	2140	4533	4532
474	2143	2142	4535	4534
475	2145	2144	4537	4536

·	WO 99/28475		206		PCT/IB98/0193
	ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
	476	2147	2146	4539	4538
	477	2149	2148	4541	4540
	478	2151	2150	4543	4542
	479	2153	2152	4545	4544
	480	2155	2154	4547	4546
	481	2157	2156	4549	4548
	482	2159	2158	4551	4550
	483	2161	2160	4553	4552
	484	2163	2162	4555	4554
	485	2165	2164	4557	4556
	486	2167	2166	4559	4558
	487	2169	2168	4561	4560
	488	2171	2170	4563	4562
	489	2173	2172	4565	4564
	490	2175	2174	4567	4566
	491	2177	2176	4569	4568
	492	2179	2178	4571	4570
	493	2181	2180	4573	4572
	494	2183	2182	4575	4574
	495	2185	2184	4577	4576
	496	2187	2186	4579	4578
	497	2189	2188	4581	4580
	498	2191	2190	4583	4582
	499	2193	2192	4585	4584
	500	2195	2194	4587	4586
	501	2197	2196	4589	4588
	502	2199	2198	4591	4590
	503	2201	2200	4593	4592
	504	2203	2202	4595	4594
	505	2205	2204	4597	4596
	506	2207	2206	4599	4598
	507	2209	2208	4601	4600
	508	2211	2210	4603	4602
	509	2213	2212	4605	4604

ORFGenset	OPENHANEA	207	OPT-1:	
	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
510	2215	2214	4607	4606
511	2217	2216	4609	4608
512	2219	2218	4611	4610
513	2221	2220	4613	4612
514	2223	2222	4615	4614
515	2225	2224	4617	4616
516	2227	2226	4619	4618
517	2229	2228	4621	4620
518	2231	2230	4623	4622
519	2233	2232	4625	4624
520	2235	2234	4627	4626
521	2237	2236	4629	4628
522	2239	2238	4631	4630
523	2241	2240	4633	4632
524	2243	2242	4635	4634
525	2245	2244	4637	4636
526	2247	2246	4639	4638
527	2249	2248	4641	4640
528	2251	2250	4643	4642
529	2253	2252	4645	4644
530	2255	2254	4647	4646
531	2257	2256	4649	4648
532	2259	2258	4651	4650
533	2261	2260	4653	4652
534	2263	2262	4655	4654
535	2265	2264	4657	4656
536	2267	2266	4659	4658
537	2269	2268	4661	4660
538	2271	2270	4663	4662
539	2273	2272	4665	4664
540	2275	2274	4667	4666
541	2277	2276	4669	4668
542	2279	2278	4671	4670
543	2281	2280	4673	4672
				-TU/L

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
544	2283	2282	4675	4674
545	2285	2284	4677	4676
546	2287	2286	4679	4678
547	2289	2288	4681	4680
548	2291	2290	4683	4682
549	2293	2292	4685	4684
550	2295	2294	4687	4686
551	2297	2296	4689	4688 -
552	2299	2298	4691	4690
553	2301	2300	4693	4692
554	2303	2302	4695	4694
555	2305	2304	4697	4696
556	2307	2306	4699	4698
557	2309	2308	4701	4700
558	2311	2310	4703	4702
559	2313	2312	4705	4704
560	2315	2314	4707	4706
561	2317	2316	4709	4708
562	2319	2318	4711	4710
563	2321	2320	4713	4712
564	2323	2322	4715	4714
565	2325	2324	4717	4716
566	2327	2326	4719	4718
567	2329	2328	4721	4720
568	2331	2330	4723	4722
569	2333	2332	4725	4724
570	2335	2334	4727	4726
571	2337	2336	4729	4728
572	2339	2338	4731	4730
573	2341	2340	4733	4732
574	2343	2342	4735	4734
575	2345	2344	4737	4736
576	2347	2346	4739	4738
577	2349	2348	4741	4740

WO 99/28475 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
578	2351	2350	4743	4742
579	2353	2352	4745	4744
580	2355	2354	4747	4746
581	2357	2356	4749	4748
582	2359	2358	4751	4750
583	2361	2360	4753	4752
584	2363	2362	4755	4754
585	2365	2364	4757	4756
586	2367	2366	4759	4758
587	2369	2368	4761	4760
588	2371	2370	4763	4762
589	2373	2372	4765	4764
590	2375	2374	4767	4766
591	2377	2376	4769	4768
592	2379	2378	4771	4770
593	2381	2380	4773	4772
594	2383	2382	4775	4774
595	2385	2384	4777	4776
596	2387	2386	4779	4778
597	2389	2388	4781	4780
598	2391	2390	4783	4782
599	2393	2392	4785	4784
600	2395	2394	4787	4786
601	2397	2396	4789	4788
602	2399	2398	4791	4790
603	2401	2400	4793	4792
604	2403	2402	4795	4794
605	2405	2404	4797	4796
606	2407	2406	4799	4798
607	2409	2408	4801	4800
608	2411	2410	4803	4802
609	2413	2412	4805	4804
610	2415	2414	4807	4806
611	2417	2416	4809	4808

ORFGenset	ORFoligosFd	ORFöligösFp	ORFoligosBd	ORFoligosBp
612	2419	2418	4811	4810
613	2421	2420	4813	4812
614	2423	2422	4815	4814
615	2425	2424	4817	4816
616	2427	2426	4819	4818
617	2429	2428	4821	4820
618	2431	2430	4823	4822
619	2433	2432	4825	4824
620	2435	2434	4827	4826
621	2437	2436	4829	4828
622	2439	2438	4831	4830
623	2441	2440	4833	4832
624	2443	2442	4835	4834
625	2445	2444	4837	4836
626	2447	2446	4839	4838
627	2449	2448	4841	4840
628	2451	2450	4843	4842
629	2453	2452	4845	4844
630	2455	2454	4847	4846
631	2457	2456	4849	4848
632	2459	2458	4851	4850
633	2461	2460	4853	4852
634	2463	2462	4855	4854
635	2465	2464	4857	4856
636	2467	2466	4859	4858
637	2469	2468	4861	4860
638	2471	2470	4863	4862
639	2473	2472	4865	4864
640	2475	2474	4867	4866
641	2477	2476	4869	4868
642	2479	2478	4871	4870
643	2481	2480	4873	4872
644	2483	2482	4875	4874
645	2485	2484	4877	4876

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
646	2487	2486	4879	4878
647	2489	2488	4881	4880
648	2491	2490	4883	4882
649	2493	2492	4885	4884
650	2495	2494	4887	4886
651	2497	2496	4889	4888
652	2499	2498	4891	4890
653	2501	2500	4893	4892
654	2503	2502	4895	4894
655	2505	2504	4897	4896
656	2507	2506	4899	4898
657	2509	2508	4901	4900
658	2511	2510	4903	4902
659	2513	2512	4905	4904
660	2515	2514	4907	4906
661	2517	2516	4909	4908
662	2519	2518	4911	4910
663	2521	2520	4913	4912
664	2523	2522	4915	4914
665	2525	2524	4917	4916
666	2527	2526	4919	4918
667	2529	2528	4921	4920
668	2531	2530	4923	4922
669	2533	2532	4925	4924
670	2535	2534	4927	4926
671	2537	2536	4929	4928
672	2539	2538	4931	4930
673	2541	2540	4933	4932
674	2543	2542	4935	4934
675	2545	2544	4937	4936
676	2547	2546	4939	4938
677	2549	2548	4941	4940
678	2551	2550	4943	4942
679	2553	2552	4945	4944

ORFGenset	ORFóligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
680	2555	2554	4947	4946
681	2557	2556	4949	4948
682	2559	2558	4951	4950
683	2561	2560	4953	4952
684	2563	2562	4955	4954
685	2565	2564	4957	4956
686	2567	2566	4959	4958
687	2569	2568	4961	4960
688	2571	2570	4963	4962
689	2573	2572	4965	4964
690	2575	2574	4967	4966
691	2577	2576	4969	4968
692	2579	2578	4971	4970
693	2581	2580	4973	4972
694	2583	2582	4975	4974
695	2585	2584	4977	4976
696	2587	2586	4979	4978
697	2589	2588	4981	4980
698	2591	2590	4983	4982
699	2593	2592	4985	4984
700	2595	2594	4987	4986
701	2597	2596	4989	4988
702	2599	2598	4991	4990
703	2601	2600	4993	4992
704	2603	2602	4995	4994
705	2605	2604	4997	4996
706	2607	2606	4999	4998
707	2609	2608	5001	5000
708	2611	2610	5003	5002
709	2613	2612	5005	5004
710	2615	2614	5007	5006
711	2617	2616	5009	5008
712	2619	2618	5011	5010
713	2621	2620	5013	5012

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
714	2623	2622	5015	5014
715	2625	2624	5017	5016
716	2627	2626	5019	5018
717	2629	2628	5021	5020
718	2631	2630	5023	5022
719	2633	2632	5025	5024
720	2635	2634	5027	5026
721	2637	2636	5029	5028
722	2639	2638	5031	5030
723	2641	2640	5033	5032
724	2643	2642	5035	5034
725	2645	2644	5037	5036
726	2647	2646	5039	5038
727	2649	2648	5041	5040
728	2651	2650	5043	5042
729	2653	2652	5045	5044
730	2655	2654	5047	5046
731	2657	2656	5049	5048
732	2659	2658	5051	5050
733	2661	2660	5053	5052
734	2663	2662	5055	5054
735	2665	2664	5057	5056
736	2667	2666	5059	5058
737	2669	2668	5061	5060
738	2671	2670	5063	5062
739	2673	2672	5065	5064
740	2675	2674	5067	5066
741	2677	2676	5069	5068
742	2679	2678	5071	5070
743	2681	2680	5073	5072
744	2683	2682	5075	5074
745	2685	2684	5077	5076
746	2687	2686	5079	5078
747	2689	2688	5081	5080

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
748	2691	2690	5083	5082
749	2693	2692	5085	5084
750	2695	2694	5087	5086
751	2697	2696	5089	5088
752	2699	2698	5091	5090
753	2701	2700	5093	5092
754	2703	2702	5095	5094
755	2705	2704	5097	5096
756	2707	2706	5099	5098
757	2709	2708	5101	5100
758	2711	2710	5103	5102
759	2713	2712	5105	5104
760	2715	2714	5107	5106
761	2717	2716	5109	5108
762	2719	2718	5111	5110
763	2721	2720	5113	5112
764	2723	2722	5115	5114
765	2725	2724	5117	5116
766	2727	2726	5119	5118
767	2729	2728	5121	5120
768	2731	2730	5123	5122
769	2733	2732	5125	5124
770	2735	2734	5127	5126
771	2737	2736	5129	5128
772	2739	2738	5131	5130
773	2741	2740	5133	5132
774	2743	2742	5135	5134
775	2745	2744	5137	5136
776	2747	2746	5139	5138
777	2749	2748	5141	5140
778	2751	2750	5143	5142
779	2753	2752	5145	5144
780	2755	2754	5147	5146
781	2757	2756	5149	5148

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
782	2759	2758	5151	5150
783	2761	2760	5153	5152
784	2763	2762	5155	5154
785	2765	2764	5157	5156
786	2767	2766	5159	5158
787	2769	2768	5161	5160
788	2771	2770	5163	5162
789	2773	2772	5165	5164
790	2775	2774	5167	5166
791	2777	2776	5169	5168
792	2779	2778	5171	5170
793	2781	2780	5173	5172
794	2783	2782	5175	5174
795	2785	2784	5177	5176
796	2787	2786	5179	5178
797	2789	2788	5181	5180
798	2791	2790	5183	5182
799	2793	2792	5185	5184
800	2795	2794	5187	5186
801	2797	2796	5189	5188
802	2799	2798	5191	5190
803	2801	2800	5193	5192
804	2803	2802	5195	5194
805	2805	2804	5197	5196
806	2807	2806	5199	5198
807	2809	2808	5201	5200
808	2811	2810	5203	5202
809	2813	2812	5205	5204
810	2815	2814	5207	5206
811	2817	2816	5209	5208
812	2819	2818	5211	5210
813	2821	2820	5213	5212
814	2823	2822	5215	5214
815	2825	2824	5217	5216

216				
ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
816	2827	2826	5219	5218
817	2829	2828	5221	5220
818	2831	2830	5223	5222
819	2833	2832	5225	5224
820	2835	2834	5227	5226
821	2837	2836	5229	5228
822	2839	2838	5231	5230
823	2841	2840	5233	5232
824	2843	2842	5235	5234
825	2845	2844	5237	5236
826	2847	2846	5239	5238
827	2849	2848	5241	5240
828	2851	2850	5243	5242
829	2853	2852	5245	5244
830	2855	2854	5247	5246
831	2857	2856	5249	5248
832	2859	2858	5251	5250
833	2861	2860	5253	5252
834	2863	2862	5255	5254
835	2865	2864	5257	5256
836	2867	2866	5259	5258
837	2869	2868	5261	5260
838	2871	2870	5263	5262
839	2873	2872	5265	5264
840	2875	2874	5267	5266
841	2877	2876	5269	5268
842	2879	2878	5271	5270
843	2881	2880	5273	5272
844	2883	2882	5275	5274
845	2885	2884	5277	5276
846	2887	2886	5279	5278
847	2889	2888	5281	5280
848	2891	2890	5283	5282
849	2893	2892	5285	5284

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
850	2895	2894	5287	5286
851	2897	2896	5289	5288
852	2899	2898	5291 .	5290
853	2901	2900	5293	5292
854	2903	2902	• 5295	5294
855	2905	2904	5297	5296
856	2907	2906	5299	5298
857	2909	2908	5301	5300
858	2911	2910	5303	5302
859	2913	2912	5305	5304
860	2915	2914	5307	5306
861	2917	2916	5309	5308
862	2919	2918	5311	5310
863	2921	2920	5313	5312
864	2923	2922	5315	5314
865	2925	2924	5317	5316
866	2927	2926	5319	5318
867	2929	2928	5321	5320
868	2931	2930	5323	5322
869	2933	2932	5325	5324
870	2935	2934	5327	5326
871	2937	2936	5329	5328
872	2939	2938	5331	5330
873	2941	2940	5333	5332
874	2943	2942	5335	5334
875	2945	2944	5337	5336
876	2947	2946	5339	5338
877	2949	2948	5341	5340
878	2951	2950	5343	5342
879	2953	2952	5345	5344
880	2955	2954	5347	5346
881	2957	2956	5349	5348
882	2959	2958	5351	5350
883	2961	2960	5353	5352

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
884	2963	2962	5355	5354
885	2965	2964	5357	5356
886	2967	2966	5359	5358
887	2969	2968	5361	5360
888	2971	2970	5363	5362
889	2973	2972	5365	5364
890	2975	2974	5367	5366
891	2977	2976	5369	5368
892	2979	2978	5371	5370
893	2981	2980	5373	5372
894	2983	2982	5375	5374
895	2985	2984	5377	5376
896	2987	2986	5379	5378
897	2989	2988	5381	5380
898	2991	2990	5383	5382
899	2993	2992	5385	5384
900	2995	2994	5387	5386
901	2997	2996	5389	5388
902	2999	2998	5391	5390
903	3001	3000	5393	5392
904	3003	3002	5395	5394
905	3005	3004	5397	5396
906	3007	3006	5399	5398
907	3009	3008	5401	5400
908	3011	3010	5403	5402
909	3013	3012	5405	5404
910	3015	3014	5407	5406
911	3017	3016	5409	5408
912	3019	3018	5411	5410
913	3021	3020	5413	5412
914	3023	3022	5415	5414
915	3025	3024	5417	5416
916	3027	3026	5419	5418
917	3029	3028	5421	5420

WO 99/28475 219 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
918	3031	3030	5423	5422
919	3033	3032	5425	5424
920	3035	3034	5427	5426
921	3037	3036	5429	5428
922	3039	3038	5431	5430
923	3041	3040	5433	5432
924	3043	3042	5435	5434
925	3045	3044	5437	5436
926	3047	3046	5439	5438
927	3049	3048	5441	5440
928	3051	3050	5443	5442
929	3053	3052	5445	5444
930	3055	3054	5447	5446
931	3057	3056	5449	5448
932	3059	3058	5451	5450
933	3061	3060	5453	5452
934	3063	3062	5455	5454
935	3065	3064	5457	5456
936	3067	3066	5459	5458
937	3069	3068	5461	5460
938	3071	3070	5463	5462
939	3073	3072	5465	5464
940	3075	3074	5467	5466
941	3077	3076	5469	5468
942	3079	3078	5471	5470
943	3081	3080	5473	5472
944	3083	3082	5475	5474
945	3085	3084	5477	5476
946	3087	3086	5479	5478
947	3089	3088	5481	5480
948	3091	3090	5483	5482
949	3093	3092	5485	5484
950	3095	3094	5487	5486
951	3097	3096	5489	5488

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
952	3099	3098	5491	5490
953	3101	3100	5493	5492
954	3103	3102	5495	5494
955	3105	3104	5497	5496
956	3107	3106	5499	5498
957	3109	3108	5501	5500
958	3111	3110	5503	5502
959	3113	3112	5505	5504
960	3115	3114	5507	5506
961	3117	3116	5509	5508
962	3119	3118	5511	5510
963	3121	3120	5513	5512
964	3123	3122	5515	5514
965	3125	3124	5517	5516
966	3127	3126	5519	5518
967	3129	3128	5521	5520
968	3131	3130	5523	5522
969	3133	3132	5525	5524
970	3135	3134	5527	5526
971	3137	3136	5529	5528
972	3139	3138	5531	5530
973	3141	3140	5533	5532
974	3143	3142	3 5535	5534
975	3145	3144	5537	5536
976	3147	3146	5539	5538
977	3149	3148	5541	5540
978	3151	3150	5543	5542
979	3153	3152	5545	5544
980	3155	3154	5547	5546
981	3157	3156	5549	5548
982	3159	3158	5551	5550
983	3161	3160	5553	5552
984	3163	3162	5555	5554
985	3165	3164	5557	5556

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
986	3167	3166	5559	5558
987	3169	3168	5561	5560
988	3171	3170	5563	5562
989	3173	3172	5565	5564
990	3175	3174	5567	5566
991	3177	3176	5569	5568
992	3179	3178	5571	5570
993	3181	3180	5573	5572
994	3183	3182	5575	5574
995	3185	3184	5577	5576
996	3187	3186	5579	5578
997	3189	3188	5581	5580
998	3191	3190	5583	5582
999	3193	3192	5585	5584
1000	3195	3194	5587	5586
1001	3197	3196	5589	5588
1002	3199	3198	5591	5590
1003	3201	3200	5593	5592
1004	3203	3202	5595	5594
1005	3205	3204	5597	5596
1006	3207	3206	5599	5598
1007	3209	3208	5601	5600
1008	3211	3210	5603	5602
1009	3213	3212	5605	5604
1010	3215	3214	5607	5606
1011	3217	3216	5609	5608
1012	3219	3218	5611	5610
1013	3221	3220	5613	5612
1014	3223	3222	5615	5614
1015	3225	3224	5617	5616
1016	3227	3226	5619	5618
1017	3229	3228	5621	5620
1018	3231	3230	5623	5622
1019	3233	3232	5625	5624

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
1020	3235	3234	5627	5626
1021	3237	3236	5629	5628
1022	3239	3238	5631	5630
1023	3241	3240	5633	5632
1024	3243	3242	5635	5634
1025	3245	3244	5637	5636
1026	3247	3246	5639	5638
1027	3249	3248	5641	5640
1028	3251	3250	5643	5642
1029	3253	3252	5645	5644
1030	3255	3254	5647	5646
1031	3257	325ύ	5649	5648
1032	3259	3258	5651	5650
1033	3261	3260	5653	5652
1034	3263	3262	5655	5654
1035	3265	3264	5657	5656
1036	3267	3266	5659	5658
1037	3269	3268	5661	5660
1038	3271	3270	5663	5662
1039	3273	3272	5665	5664
1040	3275	3274	5667	5666
1041	3277	3276	5669	5668
1042	3279	3278	5671	5670
1043	3281	3280	5673	5672
1044	3283	3282	5675	5674
1045	3285	3284	5677	5676
1046	3287	3286	5679	5678
1047	3289	3288	5681	5680
1048	3291	3290	5683	5682
1049	3293	3292	5685	5684
1050	3295	3294	5687	5686
1051	3297	3296	5689	5688
1052	3299	3298	5691	5690
1053	3301	3300	5693	5692

WO 99/28475 223 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
1054	3303	3302	5695	5694
1055	3305	3304	5697	5696
1056	3307	3306	5699	5698
1057	3309	3308	5701	5700
1058	3311	3310	5703	5702
1059	3313	3312	5705	5704
1060	3315	3314	5707	5706
1061	3317	3316	5709	5708
1062	3319	3318	5711	5710
1063	3321	3320	5713	5712
1064	3323	3322	5715	5714
1065	3325	3324	5717	5716
1066	3327	3326	5719	5718
1067	3329	3328	5721	5720
1068	3331	3330	5723	5722
1069	3333	3332	5725	. 5724
1070	3335	3334	5727	5726
1071	3337	3336	5729	5728
1072	3339	3338	5731	5730
1073	3341	3340	5733	5732
1074	3343	3342	5735	5734
1075	3345	3344	5737	5736
1076	3347	3346	5739	5738
1077	3349	3348	5741	5740
1078	3351	3350	5743	5742
1079	3353	3352	5745	5744
1080	3355	3354	5747	5746
1081	3357	3356	5749	5748
1082	3359	3358	5751	5750
1083	3361	3360	5753	5752
1084	3363	3362	5755	5754
1085	3365	3364	5757	5756
1086	3367	3366	5759	5758
1087	3369	3368	5761	5760

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
1088	3371	3370	5763	5762
1089	3373	3372	5765	5764
1090	3375	3374	5767	5766
1091	3377	3376	5769	5768
1092	3379	3378	5771	5770
1093	3381	3380	5773	5772
1094	3383	3382	5775	5774
1095	3385	3384	5777	5776
1096	3387	3386	5779	5778
1097	3389	3388	5781	5780
1098	3391	3390	5783	5782
1099	3393	3392	5785	5784
1100	3395	3394	5787	5786
1101	3397	3396	5789	5788
1102	3399	3398	5791	5790
1103	3401	3400	5793	5792
1104	3403	3402	5795	5794
1105	3405	3404	5797	5796
1106	3407	3406	5799	5798
1107	3409	3408	5801	5800
1108	3411	3410	5803	5802
1109	3413	3412	5805	5804
1110	3415	3414	5807	5806
1111	3417	3416	5809	5808
1112	3419	3418	5811	5810
1113	3421	3420	5813	5812
1114	3423	3422	5815	5814
1115	3425	3424	5817	5816
1116	3427	3426	5819	5818
1117	3429	3428	5821	5820
1118	3431	3430	5823	5822
1119	3433	3432	5825	5824
1120	3435	3434	5827	5826
1121	3437	3436	5829	5828

WO 99/28475 225 PCT/IB98/01939

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
1122	3439	3438	5831	5830
1123	3441	3440	5833	5832
1124	3443	3442	5835	5834
1125	3445	3444	5837	5836
1126	3447	3446	5839	5838
1127	3449	3448	5841	5840
1128	3451	3450	5843	5842
1129	3453	3452	5845	5844
1130	3455	3454	5847	5846
1131	3457	3456	5849	5848
1132	3459	3458	5851	5850
1133	3461	3460	5853	5852
1134	3463	3462	5855	5854
1135	3465	3464	5857	5856
1136	3467	3466	5859	5858
1137	3469	3468	5861	5860
1138	3471	3470	5863	5862
1139	3473	3472	5865	5864
1140	3475	3474	5867	5866
1141	3477	3476	5869	5868
1142	3479	3478	5871	5870
1143	3481	3480	5873	5872
1144	3483	3482	5875	5874
1145	3485	3484	5877	5876
1146	3487	3486	5879	5878
1147	3489	3488	5881	5880
1148	3491	3490	5883	5882
1149	3493	3492	5885	5884
1150	3495	3494	5887	5886
1151	3497	3496	5889	5888
1152	3499	3498	5891	5890
1153	3501	3500	5893	5892
1154	3503	3502	5895	5894
1155	3505	3504	5897	5896

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
1156	3507	3506	5899	5898
1157	3509	3508	5901	5900
1158	3511	3510	5903	5902
1159	3513	3512	5905	5904
1160	3515	3514	5907	5906
1161	3517	3516	5909	5908
1162	3519	3518	5911	5910
1163	3521	3520	5913	5912
1164	3523	3522	5915	5914
1165	3525	3524	5917	5916
1166	3527	3526	5919	5918
1167	3529	3528	5921	5920
1168	3531	3530	5923	5922
1169	3533	3532	5925	5924
1170	3535	3534	5927	5926
1171	3537	3536	5929	5928
1172	3539	3538	5931	5930
1173	3541	3540	5933	5932
1174	3543	3542	5935	5934
1175	3545	3544	5937	5936
1176	3547	3546	5939	5938
1177	3549	3548	5941	5940
1178	3551	3550	5943	5942
1179	3553	3552	5945	5944
1180	3555	3554	5947	5946
1181	3557	3556	5949	5948
1182	3559	3558	5951	5950
1183	3561	3560	5953	5952
1184	3563	3562	5955	5954
1185	3565	3564	5957	5956
1186	3567	3566	5959	5958
1187	3569	3568	5961	5960
1188	3571	3570	5963	5962
1189	3573	3572	5965	5964

ORFGenset	ORFoligosFd	ORFoligosFp	ORFoligosBd	ORFoligosBp
1190	3575	3574	5967	5966
1191	3577	3576	5969	5968
1192	3579	3578	5971	5970
1193	3581	3580	5973	5972
1194	3583	3582	5975	5974
1195	3585	3584	5977	5976
1196	3587	3586	5979	5978
1197	3589	3588	5981	5980

TABLE 5

SEQ ID	Or.	position
1198	F	1038449
1199	F	1036517
1200	F	250
1201	F	1036965
1202	F	3011
1203	F	1123
1204	F	4907
1205	F	2996
1206	F	6379
1207	F	4483
1208	F	7837
1209	F	5961
1210	F	8351
1211	F	6467
1212	F	8705
1213	F	6834
1214	F	9598
1215	F	7709
1216	F	10134
1217	F	8248
1218	F	10990
1219	F	9060
1220	F	11823
1221	F	9946
1222	F	13236
1223	F	11410
1224	F	14529
1225	F	12643
1226	F	14668
1227	F	12813
1228	F	15747
1229	F	13844

SEQ ID	Or.	position
2793	F	785793
2794	F	789918
2795	F	788039
2796	F	790378
2797	F	788456
2798	F	791834
2799	F	789918
2800	F	793102
2801	F	791176
2802	F	793826
2803	F	791921
2804	F	794911
2805	F	793023
2806	F	795296
2807	F	793427
2808	F	796005
2809	F	794127
2810	F	796729
2811	F	794811
2812	F	797041
2813	F	795065
2814	F	797553
2815	F	795651
2816	F	797716
2817	F	795815
2818	F	798197
2819	F	796285
2820	F	799004
2821	F	797173
2822	F	799785
2823	F	797910
2824	F	800789
	į	

SEQ ID	Or.	position
4388	В	394245
4389	В	396116
4390	В	395604
4391	В	397475
4392	В	396249
4393	В	398133
4394	В	396759
4395	В	398660
4396	В	397746
4397	В	399639
4398	В	398973
4399	В	400878
4400	В	399921
4401	В	401846
4402	В	400393
4403	В	402287
4404	В	401444
4405	В	403344
4406	В	402258
4407	В	404150
4408	В	403461
4409	В	405340
4410	В	405400
4411	В	407325
4412	В	404027
4413	В	405941
4414	В	406141
4415	В	408055
4416	В	407325
4417	В	409172
4418	В	409999
4419	В	411893

1230 F 15903 1231 F 14019 1232 F 17198 1233 F 15298 1234 F 18218 1235 F 16263 1236 F 20595 1237 F 18692 1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20328 1242 F 22605 1243 F 20659 1244 F 22890 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254	SEQ ID	Or.	position
1232 F 17198 1233 F 15298 1234 F 18218 1235 F 16263 1236 F 20595 1237 F 18692 1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20328 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 29785 1256 F 29785 1257 F 27860 1258 F 30276 1259	1230	F	15903
1233 F 15298 1234 F 18218 1235 F 16263 1236 F 20595 1237 F 18692 1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20328 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259	1231	F	14019
1234 F 18218 1235 F 16263 1236 F 20595 1237 F 18692 1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20338 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260	1232	F	17198
1235 F 16263 1236 F 20595 1237 F 18692 1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20328 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261	1233	F	15298
1236 F 20595 1237 F 18692 1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20328 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262	1234	F	18218
1237 F 18692 1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20328 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1235	F	16263
1238 F 21932 1239 F 19969 1240 F 22259 1241 F 20338 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1236	F	20595
1239 F 19969 1240 F 22259 1241 F 20328 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1237	F	18692
1240 F 22259 1241 F 20338 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1238	F	21932
1241 F 20338 1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1239	F	19969
1242 F 22605 1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1240	F	22259
1243 F 20659 1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1241	F	20338
1244 F 22890 1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1242	F	22605
1245 F 20987 1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1243	F	20659
1246 F 23150 1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1244	F	22890
1247 F 21244 1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1245	F	20987
1248 F 24413 1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1246	F	23150
1249 F 22506 1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1247	F	21244
1250 F 26379 1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1248	F	24413
1251 F 24476 1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1249	F	22506
1252 F 27498 1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1250	F	26379
1253 F 25602 1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1251	F	24476
1254 F 28476 1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1252	F	27498
1255 F 26621 1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1253	F	25602
1256 F 29785 1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1254	F	28476
1257 F 27860 1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1255	F	26621
1258 F 30276 1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1256	F	29785
1259 F 28363 1260 F 31184 1261 F 29287 1262 F 31574	1257	F	27860
1260 F 31184 1261 F 29287 1262 F 31574	1258	F	30276
1261 F 29287 1262 F 31574	1259	F	28363
1262 F 31574	1260	F	31184
	1261	F	29287
1263 F 29650	1262	F	31574
	1263	F	29650

SEQ ID	Or.	position
2825		
	F	798866
2826	F	801800
2827	F	799847
2828	F	802561
2829	F	800732
2830	F	802881
2831	F	800926
2832	F	804088
2833	F	802162
2834	F	805071
2835	F	803150
2836	F	806224
2837	F	804333
2838	F	807742
2839	F	805907
2840	F	808860
2841	F	806959
2842	F	810074
2843	F	808209
2844	F	811442
2845	F	809555
2846	F	812088
2847	F	810158
2848	F	813225
2849	F	811336
2850	F	813512
2851	F	811473
2852	F	814095
2853	F	812185
2854	F	814173
2855	F	812276
2856	F	815188
2857	F	813268
2858	F	815897

SEQ ID	Or.	position
4420	В	411645
4421	В	413542
4422	В	413693
4423	В	415530
4424	В	413693
4425	В	415559
4426	В	414172
4427	В	416072
4428	В	415337
4429	В	417275
4430 .	В	414599
4431	В	416499
4432	В	416887
4433	В	418821
4434	В	417700
4435	В	419585
4436	В	418274
4437	В	420173
4438	В	418823
4439	В	420732
4440	В	419778
4441	В	421678
4442	В	420461
4443	В	422361
4444	В	421460
4445	В	423336
4446	В	422265
4447	В	424120
4448	В	423263
4449	В	425182
4450	В	425302
4451	В	427252
4452	В	426283
4453	В	428210

SEQ ID	Or.	position
1264	F	33095
1265	F	31184
1266	F	33840
1267	F	31949
1268	F	34769
1269	F	32869
1270	F	34915
1271	F	32961
1272	F	35696
1273	F	33793
1274	F	36794
1275	F	34893
1276	F	37960
1277	F	36085
1278	F	38924
1279	F	37017
1280	F	39704
1281	F	37754
1282	F	40541
1283	F	38615
1284	F	41945
1285	F	40054
1286	F	42779
1287	F	40859
1288	F	43991
1289	F	42061
1290	F	45056
1291	F	43155
1292	F	45755
1293	F	43821
1294	F	46272
1295	F	44382
1296	F	46654
1297	F	44763

	250	
SEQ ID	Or.	position
2859	F	813968
2860	F	817367
2861	F	815456
2862	F	819089
2863	F	817201
2864	F	819482
2865	F	817563
2866	F	820143
2867	F	818252
2868	F	820800
2869	F	818900
2870	F	821426
2871	F	819500
2872	F	821943
2873	F	820003
2874	F	822811
2875	F	820926
2876	F	824117
2877	F	822214
2878	F	825659
2879	F	823747
2880	F	826112
2881	F	824151
2882	F	826773
2883	F	824894
2884	F	826945
2885	F	825061
2886	F	827754
2887	F	825869
2888	F	829117
2889	F	827236
2890	F	830870
2891	F	828917
2892	F	831522

SEQ ID	10-	position.
	Or.	position
4454	В	427252
4455	В	429129
4456	В	428040
4457	В	429940
4458	В	430106
4459	В	432063
4460	В	430580
4461	В	432480
4462	В	430860
4463	В	432776
4464	В	432063
4465	В	433919
4466	В	432263
4467	В	434137
4468	В	434730
4469	В	436671
4470	В	436671
4471	В	438495
4472	В	436803
4473	В	438696
4474	В	437953
4475	В	439850
4476	В	438490
4477	В	440383
4478	В	439374
4479	В	441289
4480	В	439562
4481	В	441466
4482	В	439976
4483	В	441847
4484	В	441301
4485	В	443216
4486	В	442161
4487	В	444066

SEQ ID	Or.	position
1298	F	47926
1299	F	46059
1300	F	48403
1301	F	46485
1302	F	49871
1303	F	47980
1304	F	50706
1305	F	48792
1306	F	52129
1307	F	50199
1308	F	53247
1309	F	51346
1310	F	54376
1311	F	52462
1312	F	54790
1313	F	52890
1314	F	55404
1315	F	53540
1316	F	56602
1317	F	54695
1318	F	58151
1319	F	56284
1320	F	58965
1321	F	57039
1322	F	59955
1323	F	58032
1324	F	61247
1325	F	59364
1326	F	62249
1327	F	60375
1328	F	63117
1329	F	61247
1330	F	63829
1331	F	61908

SEQ ID	Or.	position
2893	F	829613
2894	F	831995
2895	F	830093
2896	F	832585
2897	F	830686
2898	F	833149
2899	F	831240
2900	F	833660
2901	F	831704
2902	F	834442
2903	F	832539
2904	F	835147
2905	F	833252
2906	F	835536
2907	F	833656
2908	F	836378
2909	F	834480
2910	F	836990
2911	F	835067
2912	F	838512
2913	F	836603
2914	F	839718
2915	F	837811
2916	F	840211
2917	F	838266
2918	F	841434
2919	F	839485
2920	F	842250
2921	F	840377
2922	F	842761
2923	F	840912
2924	F	843000
2925	F	841103
2926	F	843583
· · · · · · · · · · · · · · · · · · ·		

GEO TO	10	
SEQ ID	Or.	
4488	В	442834
4489	В	444713
4490	В	446608
4491	В	448508
4492	В	448288
4493	В	450225
4494	В	449798
4495	В	451705
4496	В	451345
4497	В	453199
4498	В	451891
4499	В	453768
4500	В	452813
4501	В	454720
4502	В	453439
4503	В	455315
4504	В	455088
4505	В	456988
4506	В	455682
4507	В	457551
4508	В	456302
4509	В	458221
4510	В	457645
4511	В	459519
4512	В	458699
4513	В	460570
4514	В	459867
4515	В	461758
4516	В	461464
4517	В	463337
4518	В	461887
4519	В	463795
4520	В	462842
4521	В	464780

SEQ ID	Or.	position
1332	F	64066
1333	F	62136
1334	F	64369
1335	F	62437
1336	F	65124
1337	F	63225
1338	F	67407
1339	F	65513
1340	F	68652
1341	F	66758
1342	F	68946
1343	F	67080
1344	F	69660
1345	F	67818
1346	F	70432
1347	F	68572
1348	F	70866
1349	F	68946
1350	F	73272
1351	F	71373
1352	F	74657
1353	F	72752
1354	F	75282
1355	F	73383
1356	F	76781
1357	F	74878
1358	F	76925
1359	F	75017
1360	F	77935
1361	F	76028
1362	F	79611
1363	F	77750
1364	F	82371
1365	F	80509

232		
SEQ ID	Or.	position
2927	F	841683
2928	F	845985
2929	F	844098
2930	F	847919
2931	F	846025
2932	F	850011
2933	F	848109
2934	F	851442
2935	F	849547
2936	F	853479
2937	F	851567
2938	F	854701
2939	F	852801
2940	F	855197
2941	F	853282
2942	F	856012
2943	F	854111
2944	F	857227
2945	F	855326
2946	F	859309
2947	F	857458
2948	F	859418
2949	F	857515
2950	F	860468
2951	F	858583
2952	F	861361
2953	F	859441
2954	F	861872
2955	F	859979
2956	F	863352
2957	F	861444
2958	F	863777
2959	F	861872
2960	F	864636

SEQ ID	Or.	position
4522	B	464031
		465946
4523	В	
4524	В	464849
4525	В	466801
4526	В	466078
4527	В	467968
4528	В	467670
4529	В	469540
4530	В	469208
4531	В	471075
4532	В	469520
4533	В	471400
4534	В	469895
4535	В	471798
4536	В	471533
4537	В	473363
4538	В	471867
4539	В	473744
4540	В	473542
4541	В	475387
4542	В	473919
4543	В	475824
4544	В	474747
4545	В	476666
4546	В	475493
4547	В	477373
4548	В	476747
4549	В	478682
4550	В	478861
4551	В	480821
4552	В	479311
4553	В	481243
4554	В	479943
4555	В	481858

1366 F 83502 1367 F 81655 1368 F 84657 1369 F 82740 1370 F 87093 1371 F 85186 1372 F 87188 1373 F 85320 1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F	SEQ ID	Or	position
1368 F 84657 1369 F 82740 1370 F 87093 1371 F 85186 1372 F 87188 1373 F 85320 1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 94392 1393 F 92508 1394 F 97894 1395	1366	F	83502
1369 F 82740 1370 F 87093 1371 F 85186 1372 F 87188 1373 F 85320 1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396	1367	F	81655
1370 F 87093 1371 F 85186 1372 F 87188 1373 F 85320 1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396	1368	F	84657
1371 F 85186 1372 F 87188 1373 F 85320 1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1398	1369	F	82740
1372 F 87188 1373 F 85320 1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1398 F 100117	1370	F	87093
1373 F 85320 1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1398 F	1371	F	85186
1374 F 88179 1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1372	F	87188
1375 F 86281 1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 98502 1397 F 96620 1398 F 100117	1373	F	85320
1376 F 88486 1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1398 F 100117	1374	F	88179
1377 F 86598 1378 F 89077 1379 F 87236 1380 F 89495 1381 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1375	F	86281
1378 F 89077 1379 F 87236 1380 F 89495 1381 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1376	F	88486
1379 F 87236 1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1377	F	86598
1380 F 89495 1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1378	F	89077
1381 F 87578 1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1379	F	87236
1382 F 91202 1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 98502 1397 F 96620 1398 F 100117	1380	F	89495
1383 F 89232 1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1381	F	87578
1384 F 91526 1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1382	F	91202
1385 F 89598 1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1383	F	89232
1386 F 92085 1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1384	F	91526
1387 F 90203 1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1385	F	89598
1388 F 93104 1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1386	F	92085
1389 F 91239 1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1387	F	90203
1390 F 93833 1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1388	F	93104
1391 F 91938 1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1389	F	91239
1392 F 94392 1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1390	F	93833
1393 F 92508 1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1391	F	91938
1394 F 97894 1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1392	F	94392
1395 F 95984 1396 F 98502 1397 F 96620 1398 F 100117	1393	F	92508
1396 F 98502 1397 F 96620 1398 F 100117	1394	F	97894
1397 F 96620 1398 F 100117	1395	F	95984
1398 F 100117	1396	F	98502
	1397	F	96620
1399 F 98215	1398	F	100117
	1399	F	98215

SEQ ID	Or.	position
2961	F	862792
2962	F	866084
2963	F	864184
2964	F	866443
2965	F	864500
2966	F	867576
2967	F	865673
2968	F	868841
2969	F	866960
2970	F	869050
2971	F	867150
2972	F	871062
2973	F	869138
2974	F	872210
2975	F	870310
2976	F	872497
2977	F	870597
2978	F	873141
2979	F	871236
2980	F	873800
2981	F	871909
2982	F	874558
2983	F	872648
2984	F	875521
2985	F	873612
2986	F	876781
2987	F	874848
2988	F	877657
2989	F	875727
2990	F	877935
2991	F	876044
2992	F	878633
2993	F	876695
2994	F	878886

4556 B 480257 4557 B 482146 4558 B 481708 4559 B 483633 4560 B 481969 4561 B 483871 4562 B 483668 4563 B 485559 4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 487859 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4581 B 495864 4582 B 494929 <t< th=""><th>SEQ ID</th><th>Or.</th><th>position</th></t<>	SEQ ID	Or.	position
4558 B 481708 4559 B 483633 4560 B 481969 4561 B 483871 4562 B 483668 4563 B 485559 4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 487859 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 <t< td=""><td>4556</td><td>В</td><td>480257</td></t<>	4556	В	480257
4559 B 483633 4560 B 481969 4561 B 483871 4562 B 483668 4563 B 485559 4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 <t< td=""><td>4557</td><td>В</td><td>482146</td></t<>	4557	В	482146
4560 B 481969 4561 B 483871 4562 B 483668 4563 B 485559 4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 485945 4569 B 48759 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490677 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 493113 4579 B 493035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 495585	4558	В	481708
4561 B 483871 4562 B 483668 4563 B 485559 4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490677 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 493113 4579 B 493035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 495585 4587 B 497485 <td>4559</td> <td>В</td> <td>483633</td>	4559	В	483633
4562 B 483668 4563 B 485559 4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 495585 4587 B 497485 <td>4560</td> <td>В</td> <td>481969</td>	4560	В	481969
4563 B 485559 4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490691 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 49585 4587 B 497485	4561	В	483871
4564 B 485198 4565 B 487094 4566 B 488084 4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 49585 4587 B 497485	4562	В	483668
4565 B 487094 4566 B 488084 4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 495585 4587 B 497485	4563	В	485559
4566 B 488084 4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4564	В	485198
4567 B 489985 4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 495585 4587 B 497485	4565	В	487094
4568 B 485945 4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4566	В	488084
4569 B 487859 4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 49585 4586 B 497485	4567	В	489985
4570 B 489498 4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4568	В	485945
4571 B 491367 4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4569	В	487859
4572 B 488799 4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4570	В	489498
4573 B 490691 4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4571	В	491367
4574 B 490677 4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4572	В	488799
4575 B 492589 4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4573	В	490691
4576 B 492994 4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4574	В	490677
4577 B 494929 4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 497485	4575	В	492589
4578 B 493113 4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4576	В	492994
4579 B 495035 4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4577	В	494929
4580 B 493985 4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4578	В	493113
4581 B 495864 4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4579	В	495035
4582 B 494929 4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4580	В	493985
4583 B 496801 4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485		В	495864
4584 B 495090 4585 B 496989 4586 B 495585 4587 B 497485	4582	В	494929
4585 B 496989 4586 B 495585 4587 B 497485	4583	В	496801
4586 B 495585 4587 B 497485	4584	В	495090
4587 B 497485		В	496989
		В	495585
4500 5 40540		В	497485
	4588	В	495436
4589 B 497304	4589	В	497304

SEQ ID	Or.	position	
1400	F	101104	
1401	F	99158	
1402	F	101981	
1403	F	100080	
1404	F	102499	
1405	F	100546	
1406	F	104014	
1407	F	102126	
1408	F	105028	
1409	F	103092	
1410	F	107210	
1411	F	105310	
1412	F	108446	
1413	F	106545	
1414	F	108792	
1415	F	106853	
1416	F	109472	
1417	F	107561	
1418	F	111060	
1419	F	109147	
1420	F	112669	
1421	F	110796	
1422	F	113335	
1423	F	111435	
1424	F	113733	
1425	F	111882	
1426	F	114479	
1427	F	112580	
1428	F	115138	
1429	F	113196	
1430	F	115765	
1431	F	113891	
1432	F	119580	
1433	F	117660	
	<u> </u>		

SEQ ID	Or.	position
2995	F	876963
2996	F	879824
2997	F	877933
2998	F	880670
2999	F	878769
3000	F	881719
3001	F	879824
3002	F	882682
3003	F	880774
3004	F	883432
3005	F	881540
3006	F	884263
3007	F	882357
3008	F	884947
3009	F	883044
3010	F	888721
3011	F	886762
3012	F	890084
3013	F	888182
3014	F	890897
3015	F	888996
3016	F	891749
3017	F	889830
3018	F	893136
3019	F	891228
3020	F	893415
3021	F	891471
3022	F	893591
3023	F	891684
3023	F	894005
3025	F	892127
3025	F	894827
3027	F	892900
3028	F	895732
3020	"	33,32

ORC TE	10	L4-3
SEQ ID	Or.	position
4590	В	496854
4591	В	498754
4592	В	497396
4593	В	499316
4594	В	498735
4595	В	500635
4596	В	499484
4597	В	501409
4598	В	501005
4599	В	502852
4600	В	501937
4601	В	503853
4602	В	503083
4603	В	505003
4604	В	503895
4605	В	505846
4606	В	505263
4607	В	507137
4608	В	507214
4609	В	509106
4610	В	507687
4611	В	509559
4612	В	508632
4613	В	510534
4614	В	508863
4615	В	510730
4616	В	509202
4617	В	511062
4618	В	510940
4619	В	512832
4620	В	511747
4621	В	513649
4622	В	512446
4623	В	514305

SEQ ID	Or.	position
1434	F	123834
1435	F	121914
1436	F	124649
1437	F	122753
1438	F	125280
1439	F	123416
1440	F	126101
1441	F	124208
1442	F	126871
1443	F	125013
1444	F	127698
1445	F	125787
1446	F	129465
1447	F	127467
1448	F	130799
1449	F	128869
1450	F	131615
1451	F	129711
1452	F	132856
1453	F	130914
1454	F	133401
1455	F	131474
1456	F	133624
1457	F	131706
1458	F	134385
1459	F	132500
1460	F	137183
1461	F	135320
1462	F	140106
1463	F	138215
1464	F	140839
1465	F	138927
1466	F	141535
1467	F	139614

SEQ ID	Or.	position
3029	F	893790
3030	F	896823
3031	F	894907
3032	F	900571
3033	F	898639
3034	F	902407
3035	F	900507
3036	F	903243
3037	F	901346
3038	F	903616
3039	F	901726
3040	F	905486
3041	F	903589
3042	F	906234
3043	F	904350
3044	F	906774
3045	F	904846
3046	F	907868
3047	F	905924
3048	F	908501
3049	F	906583
3050	F	908975
3051	F	907079
3052	F	909351
3053	F	907456
3054	F	909835
3055	F	907957
3056	F	910382
3057	F	908496
3058	F	910693
3059	F	908829
3060	F	912169
3061	F	910248
3062	F	912376

SEQ ID	Or.	position
4624	В	513313
4625	В	515212
4626	В	514529
4627	В	516410
4628	В	515466
4629	В	517364
4630	В	515496
4631	В	517389
4632	В	516069
4633	В	517978
4634	В	516642
4635	В	518551
4636	В	517420
4637	В	519349
4638	В	518187
4639	В	520053
4640	В	518617
4641	В	520500
4642	В	519078
4643	В	520963
4644	В	519736
4645	В	521636
4646	В	520719
4647	В	522655
4648	В	522221
4649	В	524115
4650	В	522354
4651	В	524287
4652	В	523763
4653	В	525689
4654	В	524854
4655	В	526756
4656	В	525970
4657	В	527866

SEQ ID	Or.	position
1468	F	142909
1469	F	140952
1470	F	143684
1471	F	141782
1472	F	144309
1473	F	142375
1474	F	146178
1475	F	144294
1476	F	146894
1477	F	144997
1478	F	147858
1479	F	145960
1480	F	148277
1481	F	146347
1482	F	148781
1483	F	146846
1484	F	148947
1485	F	147021
1486	F	149424
1487	F	147592
1488	F	150769
1489	F	148884
1490	F	151743
1491	F	149880
1492	F	152659
1493	F	150769
1494	F	153101
1495	F	151270
1496	F	153719
1497	F	151850
1498	F	155002
1499	F	153096
1500	F	156550
1501	F	154687

SEQ ID	GEO TD los lastic		
	Or.	position	
3063	F	910476	
3064	F	912984	
3065	F	911084	
3066	F	913437	
3067	F	911545	
3068	F	914282	
3069	F	912376	
3070	F	914925	
3071	F	913023	
3072	F	915394	
3073	F	913510	
3074	F	915827	
3075	F	913912	
3076	F	916683	
3077	F	914788	
3078	F	917347	
3079	F	915438	
3080	F	918089	
3081	F	916189	
3082	F	918399	
3083	F	916506	
3084	F	919296	
3085	F	917406	
3086	F	919457	
3087	F	917598	
3088	F	919864	
3089	F	917963	
3090	F	920641	
3091	F	918711	
3092	F	921029	
3093	F	919138	
3094	F	921239	
3095	F	919366	
3096	F	921526	

SEQ ID	Or.	position
4658	В	526312
4659	В	528202
4660	В	526640
4661	В	528553
4662	В	526991
4663	В	528855
4664	В	528553
4665	В	530443
4666	В	529081
4667	В	530988 -
4668	В	529943
4669	В	531844
4670	В	530424
4671	В	532301
4672	В	530799
4673	В	532675
4674	В	531670
4675	В	533594
4676	В	533498
4677	В	535393
4678	В	534147
4679	В	535997
4680	В	534892
4681	В	536813
4682	В	536191
4683	В	538068
4684	В	539438
4685	В	541306
4686	В	540771
4687	В	542639
4688	В	541223
4689	В	543141
4690	В	542025
4691	В	543927

SEQ ID	Or.	position
1502	F	157206
1503	F	155353
1504	F	158818
1505	F	156924
1506	F	159676
1507	F	157795
1508	F	160957
1509	F	159063
1510	F	161319
1511	F	159504
1512	F	162131
1513	F	160240
1514	F	162775
1515	F	160865
1516	F	164236
1517	F	162345
1518	F	165837
1519	F	163923
1520	F	166508
1521	F	164605
1522	F	168612
1523	F	166683
1524	F	169367
1525	F	167436
1526	F	170556
1527	F	168661
1528	F	171067
1529	F	169173
1530	F	172090
1531	F	170171
1532	F	172797
1533	F	170904
1534	F	174176
1535	F	172236

3097 F 919638 3098 F 921930 3099 F 919979 3100 F 922212 3101 F 920325 3102 F 922925 3103 F 921029 3104 F 923258 3105 F 921324 3106 F 923808 3107 F 921929 3108 F 9241£5 3109 F 922311 3110 F 924680 3111 F 924680 3112 F 925111 3113 F 922764 3114 F 925258 3114 F 924638 3115 F 924638 3116 F 926538 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 928974 <t< th=""><th>SEQ ID</th><th>Or.</th><th>position</th></t<>	SEQ ID	Or.	position
3099 F 919979 3100 F 922212 3101 F 920325 3102 F 922925 3103 F 921029 3104 F 923258 3105 F 921324 3106 F 923808 3107 F 921929 3108 F 9241£5 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 926972 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 928974 3123 F 927031 3124 F 93003 3125 F 928103 <tr< td=""><td>3097</td><td>F</td><td>919638</td></tr<>	3097	F	919638
3100 F 922212 3101 F 920325 3102 F 922925 3103 F 921029 3104 F 923258 3105 F 921324 3106 F 923808 3107 F 921929 3108 F 924185 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926538 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 <t< td=""><td>3098</td><td>F</td><td>921930</td></t<>	3098	F	921930
3101 F 920325 3102 F 922925 3103 F 921029 3104 F 923258 3105 F 921324 3106 F 923808 3107 F 921929 3108 F 9241£5 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926538 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 928974 3122 F 928974 3123 F 927031 3124 F 93003 3125 F 928103 3126 F 930383 <tr< td=""><td>3099</td><td>F</td><td>919979</td></tr<>	3099	F	919979
3102 F 922925 3103 F 921029 3104 F 923258 3105 F 921324 3106 F 923808 3107 F 921929 3108 F 924185 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926538 3117 F 925072 3118 F 927072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 <t< td=""><td>3100</td><td>F</td><td>922212</td></t<>	3100	F	922212
3103 F 921029 3104 F 923258 3105 F 921324 3106 F 923808 3107 F 921929 3108 F 924185 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928402 3128 F 931084 3129 F 929222	3101	F	920325
3104 F 923258 3105 F 921324 3106 F 923808 3107 F 921929 3108 F 9241£5 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222 <td>3102</td> <td>·F</td> <td>922925</td>	3102	·F	922925
3105 F 921324 3106 F 923808 3107 F 921929 3108 F 9241£5 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3103	F	921029
3106 F 923808 3107 F 921929 3108 F 9241E5 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3104	F	923258
3107 F 921929 3108 F 9241£5 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3105	F	921324
3108 F 9241E5 3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3106	F	923808
3109 F 922311 3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3107	F	921929
3110 F 924680 3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3108	F	924185
3111 F 922764 3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3109	F	922311
3112 F 925111 3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3110	F	924680
3113 F 923258 3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3111	F	922764
3114 F 926538 3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3112	F	925111
3115 F 924638 3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3113	F	923258
3116 F 926972 3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3114	F	926538
3117 F 925072 3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3115	F	924638
3118 F 927351 3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3116	F	926972
3119 F 925415 3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3117	F	925072
3120 F 927870 3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3118	F	927351
3121 F 925924 3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3119	F	925415
3122 F 928974 3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3120	F	927870
3123 F 927031 3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3121	F	925924
3124 F 930003 3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3122	F	928974
3125 F 928103 3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3123	F	927031
3126 F 930383 3127 F 928402 3128 F 931084 3129 F 929222	3124	F	930003
3127 F 928402 3128 F 931084 3129 F 929222		F	928103
3128 F 931084 3129 F 929222		F	930383
3129 F 929222		F	928402
		F	931084
3130 F 931307		F	
	3130	F	931307

4692 B 543495 4693 B 545375 4694 B 544367 4695 B 546253 4696 B 544790 4697 B 546697 4698 B 544982 4699 B 546890 4700 B 548555 4701 B 548555 4702 B 547609 4703 B 549667 4704 B 547609 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 553750 4716 B 555165 4719 B 556590 4721 B 558489 <t< th=""><th>SEQ ID</th><th>Or.</th><th>position</th></t<>	SEQ ID	Or.	position
4694 B 544367 4695 B 546253 4696 B 544790 4697 B 546697 4698 B 544982 4699 B 546890 4700 B 546655 4701 B 548555 4702 B 547701 4703 B 549667 4704 B 549667 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 553750 4716 B 553750 4718 B 555165 4719 B 556590 4720 B 558489 4721 B 558489 <t< td=""><td>4692</td><td>В</td><td>543495</td></t<>	4692	В	543495
4695 B 546253 4696 B 544790 4697 B 546697 4698 B 546890 4700 B 546655 4701 B 548555 4702 B 547701 4703 B 549667 4704 B 549533 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 559024 4724 B 558346 <td>4693</td> <td>В</td> <td>545375</td>	4693	В	545375
4696 B 544790 4697 B 546697 4698 B 544982 4699 B 546890 4700 B 546655 4701 B 548555 4702 B 547701 4703 B 549667 4704 B 549667 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 559024 4724 B 558346 <td>4694</td> <td>В</td> <td>544367</td>	4694	В	544367
4697 B 546697 4698 B 544982 4699 B 546890 4700 B 546655 4701 B 548555 4702 B 547701 4703 B 549667 4704 B 549609 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 555165 4718 B 555165 4719 B 556590 4720 B 558489 4721 B 558489 4722 B 559024 4724 B 558346 <td>4695</td> <td>В</td> <td>546253</td>	4695	В	546253
4698 B 544982 4699 B 546890 4700 B 546655 4701 B 548555 4702 B 547701 4703 B 549667 4704 B 549667 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 557075 4720 B 558489 4721 B 558489 4722 B 559024 4724 B 558346	4696	В	544790
4699 B 546890 4700 B 546655 4701 B 548555 4702 B 547701 4703 B 549667 4704 B 547609 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4697	В	546697
4700 B 546655 4701 B 548555 4702 B 547701 4703 B 549667 4704 B 549667 4704 B 549667 4704 B 549609 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 558346	4698	В	544982
4701 B 548555 4702 B 547701 4703 B 549667 4704 B 547609 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 557075 4720 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4699	В	546890
4702 B 547701 4703 B 549667 4704 B 549667 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4700	В	546655
4703 B 549667 4704 B 547609 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553261 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4701	В	548555
4704 B 547609 4705 B 549533 4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553261 4716 B 553261 4717 B 555176 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 557130 4723 B 558346	4702	В	547701
4705 B 549533 4706 B 548121 4707 B 550040 4708 B 550040 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4703	В	549667
4706 B 548121 4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4704	В	547609
4707 B 550040 4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 557130 4723 B 558346	4705	В	549533
4708 B 548878 4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4706	В	548121
4709 B 550836 4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 557130 4723 B 559024 4724 B 558346	4707	В	550040
4710 B 549681 4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 559024 4724 B 558346	4708	В	548878
4711 B 551602 4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 556590 4721 B 558489 4722 B 557130 4723 B 558346	4709	В	550836
4712 B 550605 4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346	4710	В	549681
4713 B 552527 4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555165 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	551602
4714 B 551849 4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346	4712	В	550605
4715 B 553750 4716 B 553261 4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	552527
4716 B 553261 4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	551849
4717 B 555165 4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	
4718 B 555176 4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	553261
4719 B 557075 4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	555165
4720 B 556590 4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	555176
4721 B 558489 4722 B 557130 4723 B 559024 4724 B 558346		В	557075
4722 B 557130 4723 B 559024 4724 B 558346		В	556590
4723 B 559024 4724 B 558346		В	558489
4724 B 558346			
		В	559024
4725 B 560246			
	4725	В	560246

SEQ ID	Or.	position
1536	F	175048
1537	F	173138
1538	F	175476
1539	F	173595
1540	F	177183
1541	F	175275
1542	F	177858
1543	F	175942
1544	F	179819
1545	F	177923
1546	F	180412
1547	F	178455
1548	F	181169
1549	F	179226
1550	F	182628
1551	F	180694
1552	F	183403
1553	F	181494
1554	F	184577
1555	F	182628
1556	F	185763
1557	F	183843
1558	F	186496
1559	F	184614
1560	F	187187
1561	F	185262
1562	F	188542
1563	F	186632
1564	F	189410
1565	F	187514
1566	F	190016
1567	F	188083
1568	F	190545
1569	F	188666

SEQ ID	Or.	position
3131	F	929397
3132	F	931824
3133	F	929927
3134	F	932352
3135	F	930470
3136	F	933044
3137	F	931084
3138	F	933303
3139	F	931396
3140	F	933626
3141	F	931686
3142	F	934320
3143	F	932412
3144	F	936427
3145	F	934508
3146	F	938309
3147	F	936402
3148	F	939110
3149	F	937204
3150	F	940791
3151	F	938889
3152	F	941806
3153	F	939906
3154	F	944314
3155	F	942412
3156	F	944987
3157	F	943090
3158	F	946072
3159	F	944166
3160	F	946877
3161	F	944986
3162	F	948258
3163	F	946403
3164	F	949037

SEQ ID	Or.	position
4726	В	558455
4727	В	560376
4728	В	559450
4729	В	561362
4730	В	561581
4731	В	563478
4732	В	563153
4733	В	565073
4734	В	564319
4735	В	566220
4736	В	564201
4737	В	566078
4738	В	567243
4739	В	569143
4740	В	568192
4741	В	570133
4742	В	570619
4743	В	572532
4744	В	572241
4745	В	574208
4746	В	572994
4747	В	574916
4748	В	573744
4749	В	575640
4750	В	573679
4751	В	575571
4752	В	574398
4753	В	576288
4754	В	574677
4755	В	576633
4756	В	575033
4757	В	576922
4758	В	575482
4759	В	577363

SEQ ID	Or.	position
1570	F	191538
1571	F	189595
1572	F	192173
1573	F	190247
1574	F	193015
1575	F	191135
1576	F	194471
1577	F	192522
1578	F	194946
1579	F	193015
1580	F	196798
1581	F	194896
1582	F	197440
1583	F	195550
1584	F	197440
1585	F	195549
1586	F	198736
1587	F	196802
1588	F	199722
1589	F	197822
1590	F	200003
1591	F	198147
1592	F	200361
1593	F	198453
1594	F	200945
1595	F	199009
1596	F	202122
1597	F	200215
1598	F	203251
1599	F	201352
1600	F	203807
1601	F	201903
1602	F	206555
1603	F	204669

SEQ ID	Or.	position
3165	F	947137
3166	F	949581
3167	F	947671
3168	F	950455
3169	F	948558
3170	F	951058
3171	F	949151
3172	F	951569
3173	F	949653
3174	F	953340
3175	F	951431
3176	F	954174
3177	F	952288
3178	F	955475
3179	F	953604
3180	F	957601
3181	F	955703
3182	F	959053
3183	F	957168
3184	F	960824
3185	F	958932
3186	F	961268
3187	F	959368
3188	F	961365
3189	F	959465
3190	F	962324
3191	F	960423
3192	F	964706
3193	F	962822
3194	F	965974
3195	F	964074
3196	F	967210
3197	F	965307
3198	F	967808

SEQ ID	Or.	position
4760	В	575699
4761	В	577606
4762	В	576078
4763	В	577993
4764	В	578265
4765	В	580143
4766	В	578948
4767	В	580848
4768	В	582336
4769	В	584225
4770	В	582917
4771	В	584317
4772	В	583359
4773	В	585252
4774	В	583734
4775	В	585634
4776	В	584122
4777	В	585990
4778	В	584665
4779	В	586598
4780	В	585213
4781	В	587123
4782	В	585517
4783	В	587434
4784	В	586850
4785	В	588730
4786	В	588017
4787	В	589878
4788	В	589628
4789	В	591543
4790	В	589798
4791	В	591723
4792	В	590323
4793	В	592211

SEQ ID	Or.	position
1604	F	207269
1605	F	205369
1606	F	208293
1607	F	206395
1608	F	209252
1609	F	207345
1610	F	210330
1611	F	208414
1612	F	210632
1613	F	208694
1614	F	211151
1615	F	209255
1616	F	212650
1617	F	210756
1618	F	213920
1619	F	212036
1620	F	214535
1621	F	212635
1622	F	215003
1623	F	213077
1624	F	216641
1625	F	214772
1626	F	216869
1627	F	214961
1628	F	218145
1629	F	216218
1630	F	218461
1631	F	216576
1632	F	218960
1633	F	217044
1634	F	219646
1635	F	217772
1636	F	220257
1637	F	218379

SEQ ID	Or.	position
3199	F	965925
3200	F	969286
3201	F	967320
3202	F	970802
3203	F	968888
3204	F	972169
3205	F	970269
3206	F	973487
3207	F	971616
3208	F	974339
3209	F	972408
3210	F	974988
3211	F	973035
3212	F	976035
3213	F	974114
3214	F	976367
3215	F	974411
3216	F	976665
3217	F	974730
3218	F	977439
3219	F	975500
3220	F	977698
3221	F	975799
3222	F	978389
3223	F	976478
3224	F	978665
3225	F	976760
3226	F	979134
3227	F	977270
3228	F	979473
3229	F	977592
3230	F	980915
3231	F	979026
3232	F	982043

SEQ ID	Or.	position
4794	В	591492
4795	В	593419
4796	В	593002
4797	В	594885
4798	В	593367
4799	В	595321
4800	В	594166
4801	В	596020
4802	В	595942
4803	В	597826
4804	В	596354
4805	В	598255
4806	В	597147
4807	В	598998
4808	В	597960
4809	В	599851
4810	В	601068
4811	В	602929
4812	В	602096
4813	В	603996
4814	В	603761
4815	В	605643
4816	В	604014
4817	В	605920
4818	В	604634
4819	В	606548
4820	В	605864
4821	В	607736
4822	В	606903
4823	В	608742
4824	В	607722
4825	В	609674
4826	В	609329
4827	В	611215

SEQ ID	Or.	position
1638	F	220903
1639	F	218989
1640	F	221314
1641	F	219470
1642	F	222253
1643	F	220338
1644	F	223186
1645	F	221278
1646	F	223994
1647	F	222146
1648	F	224908
1649	F	223014
1650	F	225051
1651	F	223131
1652	F	225510
1653	F	223615
1654	F	226550
1655	F	224609
1656	F	226928
1657	F	225029
1658	F	227528
1659	F	225631
1660	F	228388
1661	F	226475
1662	F	229930
1663	F	228032
1664	F	231129
1665	F	229205
1666	F	232785
1667	F	230915
1668	F	233561
1669	F	231664
1670	F	234013
1671	F	232149

2-71		
SEQ ID	Or.	position
3233	F	980178
3234	F	983628
3235	F	981736
3236	F	984149
3237	F	982271
3238	F	985180
3239	F	983280
3240	F	985815
3241	F	983882
3242	F	986458
3243	F	984547
3244	F	987340
3245	F	985462
3246	F	987686
3247	F	985815
3248	F	988559
3249	F	986670
3250	F	989455
3251	F	987558
3252	F	993122
3253	F	991289
3254	F	993186
3255	F	991297
3256	F	993650
3257	F	991727
3258	F	994007
3259	F	992107
3260	F	995743
3261	F	993915
3262	F	996663
3263	F	994763
3264	F	998586
3265	F	996755
3266	F	999153

SEQ ID	Or.	position
4828	В	609916
4829	В	611866
4830	В	612090
4831	В	613998
4832	В	613166
4833	В	615091
4834	В	613838
4835	В	615761
4836	В	614217
4837	В	616094
4838	В	615464
4839	В	617391
4840	В	615913
4841	В	617803
4842	В	617932
4843	В	619837
4844	В	618598
4845	В	620532
4846	В	619591
4847	В	621465
4848	В	620636
4849	В	622536
4850	В	620532
4851	В	622381
4852	В	621404
4853	В	623307
4854	В	621932
4855	В	623834
4856	В	622666
4857	В	624588
4858	В	623689
4859	В	625605
4860	В	624435
4861	В	626298

SEQ ID	Or.	position
1672	F	234942
1673	F	233061
1674	F	236015
1675	F	234123
1676	F	237945
1677	F	236045
1678	F	238482
1679	F	236599
1680	F	240094
1681	F	238190
1682	F	241713
1683	F	239820
1684	F	242569
1685	F	240653
1686	F	244253
1687	F	242360
1688	F	245693
1689	F	243796
1690	F	246762
1691	F	244825
1692	F	247498
1693	F	245575
1694	F	248343
1695	F	246444
1696	F	249500
1697	F	247625
1698	F	250315
1699	F	248425
1700	F	250832
1701	F	248942
1702	F	251847
1703	F	249939
1704	F	254897
1705	F	252955

SEQ ID	Or.	position
3267	F	997253
3268	F	1000967
3269	F	999092
3270	F	1001173
3271	F	999246
3272	F	1001604
3273	F	999645
3274	F	1004159
3275	F	1002326
3276	F	1004763
3277	F	1002871
3278	F	1005160
3279	F	1003235
3280	F	1007181
3281	F	1005250
3282	F	1007561
3283	F	1005665
3284	F	1008855
3285	F	1007002
3286	F	1010205
3287	F	1008342
3288	F	1011716
3289	F	1009823
3290	F	1011812
3291	F	1009914
3292	F	1012372
3293	F	1010385
3294	F	1012567
3295	F	1010624
3296	F	1013237
3297	F	1011337
3298	F	1013690
3299	F	1011856
3300	F	1014301

SEQ ID	Or.	position
4862	В	625204
4863	В	627128
4864	В	626885
4865	В	628790
4866	В	627128
4867	В	629026
4868	В	628073
4869	В	629983
4870	В	628359
4871	В	630267
4872	В	628976
4873	В	63085C
4874	В	630023
4875	В	631988
4876	В	630642
4877	В	632526
4878	В	631205
4879	В	633081
4880	В	632046
4881	В	633969
4882	В	638311
4883	В	640204
4884	В	640448
4885	В	642328
4886	В	643695
4887	В	645639
4888	В	640847
4889	В	642769
4890	В	644745
4891	В	646615
4892	В	645686
4893	В	647558
4894	В	646060
4895	В	647972

SEQ ID	Or.	position
1706	F	256543
1707	F	254643
1708	F	257692
1709	F	255790
1710	F	258561
1711	F	256651
1712	F	258927
1713	F	257036
1714	F	261368
1715	F	259469
1716	F	263887
1717	F	262000
1718	F	264503
1719	F	262599
1720	F	265364
1721	F	263512
1722	F	266202
1723	F	264277
1724	F	266709
1725	F	264801
1726	F	267847
1727	F	265947
1728	F	267980
1729	F	266077
1730	F	268271
1731	F	266341
1732	F	269840
1733	F	267913
1734	F	270961
1735	F	269072
1736	F	271883
1737	F	270080
1738	F	272642
1739	F	270748

3301		
1	F	1012396
3302	F	1014926
3303	F	1013010
3304	F	1015664
3305	F	1013820
3306	F	1017026
3307	F	1015099
3308	F	1017674
3309	F	1015786
3310	F	1018353
3311	F	1016460
3312	F	1019602
3313	F	1017674
3314	F	1019876
3315	F	1017948
3316	F	1020853
3317	F	1018956
3318	F	1021878
3319	F	1019972
3320	F	1023054
3321	F	1021186
3322	F	1023415
3323	F	1021579
3324	F	1023748
3325	F	1021850
3326	F	1024485
3327	F	1022574
3328	F	1024744
3329	F	1022836
3330		1025618
3331	F	1023720
3332	F	1026323
3333	F	1024403
3334	F	1027710

SEQ ID	10-	
	Or.	position
4896	В	647331
4897	В	649231
4898	В	649987
4899	В	651829
4900	В	650580
4901	В	652484
4902	В	651942
4903	В	653852
4904	В	652395
4905	В	654310
4906	В	653132
4907	В	655028
4908	В	653827
4909	В	655713
4910	В	662071
4911	В	664023
4912	В	662543
4913	В	664403
4914	В	663295
4915	В	665205
4916	В	663972
4917	В	665850
4918	В	664432
4919	В	666332
4920	В	665860
4921	В	667789
4922	В	666312
4923	В	668233
4924	В	666652
4925	В	668550
4926	В	668338
4927	В	670238
4928	В	668605
4929	В	670495

SEQ ID	Or.	position
1740	F	273367
1741	F	271477
1742	F	274562
1743	F	272702
1744	F	275882
1745	F	273984
1746	F	278004
1747	F	276149
1748	F	278747
1749	·F	276893
1750	F	279521
1751	F	277632
1752	F	281076
1753	F	279118
1754	F	281551
1755	F	279668
1756	F	282573
1757	F	280663
1758	F	284229
1759	F	282316
1760	F	284598
1761	F	282655
1762	F	285418
1763	F	283518
1764	F	286104
1765	F	284229
1766	F	286456
1767	F	284531
1768	F	287865
1769	F	286008
1770	F	289163
1771	F	287384
1772	F	290609
1773	F	288709

SEQ ID	Or.	position
3335	F	1025809
3336	F	1030272
3337	F	1028389
3338	F	1031486
3339	F	1029602
3340	F	1033215
3341	F	1031334
3342	F	1035425
3343	F	1033555
3344	F	1035956
3345	F	1034055
3346	F	1036748
3347	F	1034844
3348	F	16372
3349	F	14463
3350	F	31184
3351	F	29287
3352	F	56283
3353	F	54383
3354	F	56384
3355	F	54538
3356	F	64528
3357	F	62600
3358	F	72965
3359	F	71054
3360	F	78245
3361	F	76347
3362	F	79133
3363	F	77291
3364	F	81740
3365	F	79840
3366	F	86772
3367	F	84880
3368	F	109188

SEQ ID	Or.	position
4930	В	668690
4931	В	670590
4932	В	669766
4933	В	671653
4934	В	670160
4935	В	672109
4936	В	671000
4937	В	672900
4938	В	671470
4939	В	673412
4940	В	672685
4941	В	674567
4942	В	673461
4943	В	675365
4944	В	674786
4945	В	676682
4946	В	675456
4947	В	677375
4948	В	676683
4949	В	678594
4950	В	677334
4951	В	679183
4952	В	678726
4953	В	680596
4954	В	679729
4955	В	681628
4956	В	680747
4957	В	682668
4958	В	681500
4959	В	683406
4960	В	682779
4961	В	684716
4962	В	683320
4963	В	685249

SEQ ID	Or.	position
1774	F	291264
1775	F	289389
1776	F	292107
1777	F	290166
1778	F	293099
1779	F	291211
1780	F	294791
1781	F	292883
1782	F	295464
1783	F	293573
1784	F	296018
1785	F	294095
1786	F	297572
1787	F	295664
1788	F	298686
1789	F	296716
1790	F	300305
1791	F	298407
1792	F	301852
1793	F	299946
1794	F	304754
1795	F	302849
1796	F	305854
1797	F	303992
1798	F	306214
1799	F	304303
1800	F	306758
1801	F	304856
1802	F	309057
1803	F	307125
1804	F	309635
1805	F	307750
1806	F	310491
1807	F	308597

		position
3369	F	107337
3370	F	111132
3371	F	109188
3372	F	111505
3373	F	109597
3374	F	112432
3375	F	110462
3376	F	113446
3377	F	111592
3378	F	120225
3379	F	118303
3380	F	124892
3381	F	123004
3382	F	131327
3383	F	129485
3384	F	143944
3385	F	142043
3386	F	150138
3387	F	148247
3388	F	163715
3389	F	161804
3390	F	165186
3391	F	163274
3392	F	168143
3393	F	166302
3394	F	170287
3395	F	168387
3396	F	176838
3397	F	174996
3398	F	187776
3399	F	185900
3400		188083
3401		186208
3402	F	190117

		_
SEQ ID	Or.	position
4964	В	684716
4965	В	686585
4966	В	685010
4967	В	686897
4968	В	686423
4969	В	688323
4970	В	687426
4971	В	689324
4972	В	688619
4973	В	690482
4974	В	688653
4975	В	690563
4976	В	689836
4977	В	691775
4978	В	690186
4979	В	692088
4980	В	690715
4981	В	692616
4982	В	690937
4983	В	692837
4984	В	692091
4985	В	693991
4986	В	694171
4987	В	696078
4988	В	695197
4989	В	697093
4990	В	697486
4991	В	699428
4992	В	698313
4993	В	700238
4994	В	698646
4995	В	700515
4996	В	700337
4997	В	702249

SEQ ID	Or.	position
1808	F	311753
1809	F	309790
1810	F	313188
1811	F	311292
1812	F	314121
1813	F	312194
1814	F	314489
1815	F	312539
1816	F	315431
1817	F	313526
1818	F	316309
1819	F	314380
1820	F	317102
1821	F	315214
1822	F	317271
1823	F	315343
1824	F	317380
1825	F	315480
1826	F	318256
1827	F	316352
1828	F	319047
1829	F	317181
1830	F	320325
1831	F	318338
1832	F	321228
1833	F	319366
1834	F	321676
1835	F	319782
1836	F	322066
1837	F	320097
1838	F	322910
1839	F	320982
1840	F	324744
1841	F	322849

SEQ ID	Or.	position
3403	F	188168
3404	F	196802
3405	F	194946
3406	F	210685
3407	F	208785
3408	F	234633
3409	F	232727
3410	F	236682
3411	F	234794
3412	F	249227
3413	F	247310
3414	F	252939
3415	F	251036
3416	F	253406
3417	F	251562
3418	F	271365
3419	F	269466
3420	F	275390
3421	F	273489
3422	F	277681
3423	F	275765
3424	F	282260
3425	F	280357
3426	F	292925
3427	F	291054
3428	F	302910
3429	F	301032
3430	F	308746
3431	F	306806
3432	F	311994
3433	F	310073
3434	F	312375
3435	F	310483
3436	F	312531

SEQ ID	Or.	position
4998	В	701115
4999	В	703015
5000	В	702385
5001	В	704285
5002	В	703636
5003	В	705561
5004	В	705271
5005	В	707136
5006	В	705875
5007	В	707725
5008	В	706444
5009	В	708279
5010	В	706741
5011	В	708673
5012	В	708324
5013	В	710226
5014	В	708673
5015	В	710518
5016	В	708876
5017	В	710791
5018	В	710498
5019	В	712447
5020	В	711435
5021	В	713354
5022	В	712993
5023	В	714887
5024	В	713686
5025	В	715574
5026	В	714474
5027	В	716354
5028	В	714867
5029	В	716760
5030	В	716047
5031	В	717877

SEQ ID	Or.	position
1842	F	325392
1843	F	323445
1844	F	326217
1845	F	324331
1846	F	327038
1847	F	325162
1848	F	327957
1849	F	326079
1850	F	328458
1851	F	326612
1852	F	329032
1853	F	327173
1854	F	329329
1855	F	327489
1856	F	330446
1857	F	328551
1858	F	330915
1859	F	329032
1860	F	331410
1861	F	329602
1862	F	332534
1863	F	330626
1864	F	332782
1865	F	330879
1866	F	333587
1867	F	331632
1868	F	333870
1869	F	331962
1870	F	334510
1871	F	332594
1872	F	334958
1873	F	333049
1874	F	334958
1875	F	333049

SEQ ID	Or.	position
3437	F	310647
3438	F	319923
3439	F	318009
3440	F	339991
3441	F	338104
3442	F	352535
3443	F	350653
3444	F	373218
3445	F	371320
3446	F	376994
3447	F	375085
3448	F	378954
3449	F	377011
3450	F	394604
3451	F	392704
3452	F	400915
3453	F	398972
3454	F	409744
3455	F	407904
3456	F	411155
3457	F	409253
3458	F	414197
3459	F	412281
3460	F	422638
3461	F	420770
3462	F	427595
3463	F	425701
3464	F	428453
3465	F	426553
3466	F	442272
3467	F	440364
3468	F	443303
3469	F	441380
3470	F	442939

	-,	
SEQ ID	Or.	position
5032	В	716086
5033	В	717976
5034	В	717189
5035	В	719068
5036	В	718624
5037	В	720503
5038	В	719083
5039	В	720983
5040	В	720047
5041	В	722004
5042	В	720503
5043	В	722393
5044	В	720753
5045	В	722653
5046	В	721798
5047	В	723724
5048	В	722631
5049	В	724493
5050	В	723468
5051	В	725376
5052	В	724852
5053	В	726743
5054	В	726005
5055	В	727903
5056	В	726779
5057	В	728691
5058	В	727058
5059	В	728947
5060	В	727727
5061	В	729613
5062	В	728224
5063	В	730116
5064	В	729048
5065	В	730907

SEQ ID	Or.	position
1876	F	335655
1877	F	333766
1878	F	336117
1879	F	334219
1880	F	337108
1881	F	335210
1882	F	340251
1883	F	338372
1884	F	341538
1885	F	339662
1886	F	341953
1887	F	339995
1888	F	342348
1889	F	340450
1890	F	343112
1891	F	341242
1892	F	343736
1893	F	341811
1894	F	344117
1895	F	342207
1896	F	344940
1897	F	343000
1898	F	345837
1899	F	343958
1900	F	346872
1901	F	344994
1902	F	347910
1903	F	345971
1904	F	350124
1905	F	348298
1906	F	351095
1907	F	349167
1908	F	351996
1909	F	350122

SEQ ID	Or.	position
3471	F	441047
3472	F	445572
3473	F	443707
3474	F	467757
3475	F	465801
3476	F	471583
3477	F	469712
3478	F	487813
3479	F	485913
3480	F	496852
3481	F	494952
3482	F	499979
3483	F	498074
3484	F	508715
3485	F	506798
3486	F	510584
3487	F	508632
3488	F	526255
3489	F	524350
3490	F	531098
3491	F	529150
3492	F	556575
3493	F	554706
3494	F	564318
3495	F	562390
3496	F	566692
3497	F	564838
3498	F	570033
3499	F	568150
3500	F	570844
3501	F	568915
3502	F	575571
3503	F	573671
3504	F	590045

SEQ ID	Or.	position
5066	В	729566
5067	В	731468
5068	В	732909
5069	В	734770
5070	В	734663
5071	В	736569
5072	В	735879
5073	В	737785
5074	В	736724
5075	B.	738632
5076	В	737474
5077	В	739421
5078	В	738007
5079	В	739907
5080	В	738911
5081	В	740799
5082	В	739960
5083	В	741908
5084	В	742277
5085	В	744187
5086	В	743089
5087	В	744989
5088	В	743603
5089	В	745539
5090	В	744565
5091	В	746432
5092	В	744977
5093	В	746867
5094	В	745249
5095	В	747138
5096	В	7457 7 7
5097	В	747677
5098	В	746632
5099	В	748532

SEQ ID	Or.	position
1910	F	353051
1911	F	351186
1912	F	353413
1913	F	351481
1914	F	353908
1915	F	351996
1916	F	354723
1917	F	352799
1918	F	356466
1919	F	354569
1920	F	357107
1921	F	355178
1922	F	357767
1923	F	355878
1924	F	360528
1925	F	358628
1926	F	360877
1927	F	358974
1928	F	361573
1929	F	359692
1930	F	362584
1931	F	360681
1932	F	363835
1933	F	361966
1934	F	364960
1935	F	363021
1936	F	365240
1937	F	363360
1938	F	367060
1939	F	365115
1940	F	368383
1941	F	366505
1942	F	368862
1943	F	366963

SEQ ID Or. position 3505 F 588196 3506 F 597631 3507 F 595698 3508 F 606387 3509 F 604507 3510 F 607566 3511 F 605637 3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 65262 3524 F 660587 3525 F 676785 3527 F 674938 3529 F 677133 35			
3506 F 597631 3507 F 595698 3508 F 606387 3509 F 604507 3510 F 607566 3511 F 605637 3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	SEQ ID		position
3507 F 595698 3508 F 606387 3509 F 604507 3510 F 607566 3511 F 605637 3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 758555 3535 F 756641 3536 F 760010 3537 F 758082		F	588196
3508 F 606387 3509 F 604507 3510 F 607566 3511 F 605637 3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010	3506	F	597631
3509 F 604507 3510 F 607566 3511 F 605637 3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3531 F 730091 3532 F 741797 3533 F 758555 3535 F 756641 3536 F 760010 <t< td=""><td></td><td>F</td><td>595698</td></t<>		F	595698
3510 F 607566 3511 F 605637 3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3508	F	606387
3511 F 605637 3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3531 F 730091 3532 F 741797 3533 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3509	F	604507
3512 F 609842 3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3510	F	607566
3513 F 607958 3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3511	F	605637
3514 F 632472 3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3512	F	609842
3515 F 630572 3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3513	F	607958
3516 F 636994 3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3514	F	632472
3517 F 635071 3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3515	F	630572
3518 F 649681 3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3516	F	636994
3519 F 647800 3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3517	F	635071
3520 F 652059 3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3518	F	649681
3521 F 650101 3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3519	F	647800
3522 F 654522 3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3520	F	652059
3523 F 652562 3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3521	F	650101
3524 F 660587 3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3522	F	654522
3525 F 658691 3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3523	F	652562
3526 F 676785 3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3524	F	660587
3527 F 674938 3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3525	F	658691
3528 F 679031 3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3526	F	676785
3529 F 677133 3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3527	F	674938
3530 F 731967 3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3528	F	679031
3531 F 730091 3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3529	F	677133
3532 F 741797 3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3530	F	731967
3533 F 739935 3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3531	F	730091
3534 F 758555 3535 F 756641 3536 F 760010 3537 F 758082	3532	F	741797
3535 F 756641 3536 F 760010 3537 F 758082	3533	F	739935
3536 F 760010 3537 F 758082	3534	F	758555
3537 F 758082	3535	F	756641
	3536	F	760010
3538 F 770670	3537	F	758082
	3538	F	770670

SEQ ID	To	langition.
	Or.	position
5100	В	747054
5101	В	748893
5102	В	748519
5103	В	750396
5104	В	749186
5105	В	751108
5106	В	749646
5107	В	751546
5108	В	749922
5109	В	751824
5110	В	750260
5111	В	752151
5112	В	752527
5113	В	754427
5114	В	753169
5115	В	755064
5116	В	755004
5117	В	756843
5118	В	757034
5119	В	758991
5120	В	758532
5121	В	760452
5122	В	758911
5123	В	760841
5124	В	760015
5125	В	761913
5126	В	760463
5127	В	762363
5128	В	760782
5129	В	762671
5130	В	762053
5131	В	763911
5132	В	762363
5133	В	764264

SEQ ID	Or.	position
1944	F	370513
1945	F	368631
1946	F	370974
1947	F	369076
1948	F	372891
1949	F	370980
1950	F	373395
1951	F	371495
1952	F	374005
1953	F	372033
1954	F	374474
1955	F	372572
1956	F	376509
1957	F	374624
1958	F	377630
1959	F	375708
1960	F	378384
1961	F	376507
1962	F	378798
1963	F	376871
1964	F	379413
1965	F	377501
1966	F	379890
1967	F	377989
1968	F	381241
1969	F	379348
1970	F	382485
1971	F	380579
1972	F	383395
1973	F	381536
1974	F	383730
1975	F	381782
1976	F	384948
1977	F	383057

3539 F 768751 3540 F 771896 3541 F 769996 3542 F 787857 3543 F 785958 3544 F 815714 3545 F 813840 3546 F 846380 3547 F 844470 3548 F 865673 3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 907563 3562 F 907563 3563 F 910133 3565 F 910133 3565 F 935157 <t< th=""><th>SEQ ID</th><th>Or.</th><th>position</th></t<>	SEQ ID	Or.	position
3541 F 769996 3542 F 787857 3543 F 785958 3544 F 815714 3545 F 813840 3546 F 846380 3547 F 844470 3548 F 865673 3549 F 865673 3550 F 875167 3551 F 876214 3552 F 876214 3553 F 884093 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 907563 3562 F 907563 3563 F 910133 3565 F 910133 3566 F 935157 3567 F 933211 <t< td=""><td>3539</td><td>F</td><td>768751</td></t<>	3539	F	768751
3542 F 787857 3543 F 785958 3544 F 815714 3545 F 813840 3546 F 846380 3547 F 844470 3548 F 865673 3549 F 865673 3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 907563 3562 F 907563 3563 F 905656 3564 F 910133 3565 F 910133 3566 F 935157 3567 F 933211 <t< td=""><td>3540</td><td>F</td><td>771896</td></t<>	3540	F	771896
3543 F 785958 3544 F 815714 3545 F 813840 3546 F 846380 3547 F 844470 3548 F 865673 3549 F 865673 3550 F 875167 3551 F 876214 3552 F 874314 3553 F 884093 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 910133 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 944568 <t< td=""><td>3541</td><td>F</td><td>769996</td></t<>	3541	F	769996
3544 F 815714 3545 F 813840 3546 F 846380 3547 F 844470 3548 F 867576 3549 F 865673 3550 F 875167 3551 F 876214 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 907563 3562 F 907563 3563 F 905656 3564 F 910133 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 <t< td=""><td>3542</td><td>F</td><td>787857</td></t<>	3542	F	787857
3545 F 813840 3546 F 846380 3547 F 844470 3548 F 867576 3549 F 865673 3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 907563 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664 <td>3543</td> <td>F</td> <td>785958</td>	3543	F	785958
3546 F 846380 3547 F 844470 3548 F 867576 3549 F 865673 3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3544	F	815714
3547 F 844470 3548 F 867576 3549 F 865673 3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 9072048 3562 F 907563 3563 F 907563 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 944568 3570 F 952562 3571 F 950664	3545	F	813840
3548 F 867576 3549 F 865673 3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3546	F	846380
3549 F 865673 3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3547	F	844470
3550 F 875167 3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3548	F	867576
3551 F 873254 3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3549	F	865673
3552 F 876214 3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3550	F	875167
3553 F 874314 3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3551	F	873254
3554 F 884093 3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3552	F	876214
3555 F 882162 3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3553	F	874314
3556 F 891248 3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3554	F	884093
3557 F 889348 3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3555	F	882162
3558 F 900125 3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3556	F	891248
3559 F 898298 3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3557	F	889348
3560 F 902048 3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3558	F	900125
3561 F 900125 3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3559	F	898298
3562 F 907563 3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3560	F	902048
3563 F 905656 3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3561	F	900125
3564 F 912076 3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3562	F	907563
3565 F 910133 3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3563	F	905656
3566 F 935157 3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3564	F	912076
3567 F 933211 3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3565	F	910133
3568 F 946473 3569 F 944568 3570 F 952562 3571 F 950664	3566	F	935157
3569 F 944568 3570 F 952562 3571 F 950664	3567	F	933211
3570 F 952562 3571 F 950664	3568	F	946473
3571 F 950664	3569	F	944568
	3570	F	952562
3572 F 965649	3571	F	950664
	3572	F	965649

SEQ ID	Or.	position
5134	В	763203
5135	В	765107
5136	В	764690
5137	В	766595
5138	В	765107
5139	В	766977
5140	В	766327
5141	В	768221
5142	В	766932
5143	В	768851
5144	В	768314
5145	В	770221
5146	В	769045
5147	В	770945
5148	В	770315
5149	В	772234
5150	В	770705
5151	В	772598
5152	В	770882
5153	В	772781
5154	В	771156
5155	В	773044
5156	В	772234
5157	В	774148
5158	В	773611
5159	В	775511
5160	В	774513
5161	В	776404
5162	В	776333
5163	В	778191
5164	В	777926
5165	В	779832
5166	В	777455
5167	В	779380

SEQ ID	Or.	position
1978	F	385474
1979	F	383532
1980	F	385908
1981	F	384008
1982	F	386643
1983	F	384750
1984	F	387099
1985	F	385204
1986	F	387581
1987	F	385677
1988	F	388009
1989	F	386062
1990	F	388927
1991	F	387033
1992	F	389726
1993	F	387821
1994	F	391295
1995	F	389365
1996	F	392171
1997	F	390291
1998	F	393930
1999	F	392014
2000	F	395085
2001	F	393185
2002	F	395827
2003	F	393940
2004	F	396274
2005	F	394423
2006	F	397156
2007	F	395216
2008	F	398641
2009	F	396790
2010	F	399550
2011	F	397659

SEQ ID	Or.	position
3573	F	963730
3574	F	968519
3575	F	966614
3576	F	970497
3577	F	968601
3578	F	971879
3579	F	970043
3580	F	972888
3581	F	970962
3582	F	998162
3583	F	996241
3584	F	1003657
3585	F	1001756
3586	F	1009313
3587	F	1007413
3588	F	1028954
3589	F	1027039
3590	В	730
3591	В	2645
3592	В	3521
3593	В	5431
3594	В	5295
3595	В	7188
3596	В	6740
3597	В	8652
3598	В	8240
3599	В	10138
3600	В	8959
3601	В	10816
3602	В	9285
3603	В	11160
3604	В	9689
3605	В	11591
3606	В	10679
		· · · · · · · · · · · · · · · · · · ·

SEQ ID	Or.	position
5168	B	779476
5169	В	781342
5170	В	781774
5171	В	783686
5172	В	782667
5173	В	784562
5174	В	785748
5175	В	787658
5176	В	786222
5177	В	788126
5178	В	786803
5179	В	788703
5180	В	787998
5181	В	789876
5182	В	788279
5183	В	790255
5184		790233
5185	В	792247
5186	В	790862
5187		790882
5188		792787
5189		794137
5189		
5190		793352
0_0_		795215
5192		794276
5193		796196
5194		795215
5195		797077
5196		795667
5197		797571
5198		796515
5199		798382
5200	В	797235
5201	В	799168

WO 99/28475		
SEQ ID	Or.	position
2012	F	399797
2013	F	397915
2014	F	401527
2015	F	399623
2016	F	401907
2017	F	399960
2018	F	403017
2019	F	401131
2020	F	403017
2021	F	401131
2022	F	404910
2023	F	403010
2024	F	405728
2025	F	403836
2026	F	406837
2027	F	404932
2028	F	410291
2029	F	408347
2030	F	411488
2031	F	409518
2032	F	412379
2033	F	410487
2034	F	413164
2035	F	411263
2036	F	413606
2037	F	411626
2038	F	413721
2039	F	411859
2040	F	414921
2041	F	413049
2042	F	416517
2043	F	414606
2044	F	417445

2045

415557

	202			
SEQ ID	Or.	position		
3607	В	12568		
3608	В	11515		
3609	В	13376		
3610	В	12136		
3611	В	14038		
3612	В	13565		
3613	В	15450		
3614	В	14667		
3615	В	16535		
3616	В	15254		
3617	В	17183		
3618	В	16189		
3619	В	18097		
3620	В	16790		
3621	В	18621		
3622	В	16710		
3623	В	18587		
3624	В	18458		
3625	В	20318		
3626	В	20768		
3627	В	22647		
3628	В	22438		
3629	В	24335		
3630	В	22892		
3631	В	24752		
3632	В	23046		
3633	В	24924		
3634	В	23442		
3635	В	25313		
3636	В	23623		
3637	В	25528		
3638	В	24822		
3639	В	26708		
3640	В	26618		

SEQ ID	Or.	position
5202	В	797585
5203	В	799553
5204	В	798102
5205	В	799976
5206	В	798306
5207	В	800214
5208	В	798662
5209	В	800546
5210	В	799168
5211	В	801074
5212	В	800159
5213	В	802054
5214	В	801153
5215	В	803031
5216	В	802363
5217	В	804257
5218	В	802893
5219	В	804802
5220	В	803466
5221	В	805366
5222	В	804440
5223	В	806374
5224	В	805576
5225	В	807523
5226	В	806511
5227	В	808410
5228	В	808305
5229	В	810207
5230	В	809229
5231	В	811164
5232	В	810700
5233	В	812581
5234	В	811825
5235	В	813787

PCT/IB98/01939

SEQ ID	Or.	position
2046	F	417812
2047	F	415912
2048	F	418381
2049	F	416517
2050	F	419453
2051	F	417447
2052	F	420026
2053	F	418068
2054	F	421270
2055	F	419392
2056	F	422262
2057	F	420364
2058	F	423007
2059	F	421107
2060	F	424834
2061	F	423018
2062	F	426026
2063	F	424110
2064	F	426883
2065	F	425040
2066	F	429303
2067	F	427438
2068	F	429609
2069	F	427737
2070	F	430104
2071	F	428191
2072	F	430622
2073	F	428814
2074	F	431439
2075	F	429537
2076	F	431968
2077	F	430108
2078	F	434401
2079	F	432485

SEQ ID	Or.	position
3641	В	28544
3642	В	27972
3643	В	29859
3644	В	29000
3645	В	30908
3646	В	30242
3647	В	32160
3648	В	30966
3649	В	32849
3650	В	31516
3651	В	33401
3652	В	32032
3653	В	33900
3654	В	33576
3655	В	35496
3656	В	34121
3657	В	36052
3658	В	35251
3659	В	37164
3660	В	35588
3661	В	37502
3662	В	36152
3663	В	38041
3664	В	37216
3665	В	39127
3666	В	38041
3667	В	39980
3668	В	39322
3669	В	41205
3670	В	40161
3671	В	42074
3672	В	40985
3673		42887
3674	В	42284

SEQ ID	Or.	position
5236	В	812574
5237	В	814467
5238	В	813787
5239	В	815676
5240	В	814082
5241	В	815892
5242	В	814571
5243	В	816454
5244	В	815441
5245	В	817347
5246	В	815101
5247	В	817025
5248	В	815953
5249	В	817887
5250	В	817709
5251	В	819618
5252	В	819559
5253	В	821442
5254	В	819933
5255	В	821846
5256	В	820622
5257	В	822548
5258	В	821281
5259	В	823181
5260	В	821778
5261	В	823666
5262	В	822494
5263	В	824387
5264	В	823155
5265	В	825057
5266	В	824589
5267		826509
5268		826122
5269	В	828041

SEQ ID	Or.	position
2080	F	436050
2081	F	434134
2082	F	436342
2083	F	434428
2084	F	437672
2085	F	435775
2086	F	438051
2087	F	436165
2088	F	438767
2089	F	436866
2090	F	439139
2091	F	437145
2092	F	439479
2093	F	437574
2094	F	440823
2095	F	438923
2096	F	441668
2097	F	439746
2098	F	444271
2099	F	442371
2100	F	446233
2101	F	444302
2102	F	447687
2103	F	445803
2104	F	450318
2105	F	448399
2106	F	450876
2107	F	449025
2108	F	451274
2109	F	449397
2110	F	452413
2111	F	450513
2112	F	453303
2113	F	451427

SEQ ID	Or.	position
3675	В	44180
3676	В	43337
3677	В	45275
3678	В	44022
3679	В	45927
3680	В	45451
3681	В	47375
3682	В	46308
3683	В	48208
3684	В	46560
3685	В	48485
3686	В	47115
3687	В	49053
3688	В	48208
3689	В	50118
3690	В	48806
3691	В	50708
3692	В	50333
3693	В	52220
3694	В	50960
3695	В	52890
3696	В	52660
3697	В	54606
3698	В	53737
3699	В	55645
3700	В	54793
3701	В	56691
3702	В	55329
3703	В	57226
3704	В	56691
3705	В	58566
3706	В	56317
3707	В	58226
3708	В	58469

SEQ ID	Or.	position
5270	В	826572
5271	В	828500
5272	В	827246
5273	В	829208
5274	В	827489
5275	В	829407
5276	В	828274
5277	В	830176
5278	В	829495
5279	В	831395
5280	В	831192
5281	В	833082
5282	В	832005
5283	В	833870
5284	В	832373
5285	В	834280
5286	В	832964
5287	В	834864
5288	В	833672
5289	В	835604
5290	В	834022
5291	В	835945
5292	В	834907
5293	В	836803
5294	В	835683
5295	В	837593
5296	В	836018
5297	В	837902
5298	В	836714
5299	В	838602
5300	В	837484
5301	В	839424
5302	В	838950
5303	В	840832

SEQ ID	Or.	position
2114	F	454713
2115	F	452853
2116	F	455096
2117	F	453248
2118	F	455808
2119	F	453928
2120	F	457440
2121	F	455488
2122	F	458282
2123	F	456354
2124	F	459558
2125	F	457686
2126	F	460960
2127	F	459060
2128	F	461659
2129	F	459758
2130	F	462674
2131	F	460775
2132	F	463788
2133	F	461895
2134	F	464479
2135	F	462602
2136	F	465882
2137	F	463989
2138	F	467200
2139	F	465300
2140	F	468680
2141	F	466787
2142	F	469130
2143	F	467224
2144	F	469572
2145	F	467707
2146	F	470887
2147	F	468984

3709 B 60363 3710 B 59406 3711 B 61301 3712 B 60450 3713 B 62316 3714 B 61722 3715 B 63603 3716 B 62585 3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 6997 3731 B 71354 3732 B 69470 3733 B 71898 3736 B 70707 3737	SEQ ID	Or.	position
3711 B 61301 3712 B 60450 3713 B 62316 3714 B 61722 3715 B 63603 3716 B 62585 3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71898 3734 B 69961 3735 B 72579 3738 B 71249 3739	3709	В	60363
3712 B 60450 3713 B 62316 3714 B 61722 3715 B 63603 3716 B 62585 3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71898 3734 B 69961 3735 B 72579 3738 B 71249 3739 B 73458 3741	3710	В	59406
3713 B 62316 3714 B 61722 3715 B 63603 3716 B 62585 3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71898 3734 B 69961 3735 B 72579 3738 B 71249 3739 B 73458 3741 B 75376	3711	В	61301
3714 B 61722 3715 B 63603 3716 B 62585 3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71898 3734 B 69961 3735 B 71898 3736 B 70707 3738 B 71249 3739 B 73458 3740 B 73458 3741	3712	В	60450
3715 B 63603 3716 B 62585 3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3738 B 71249 3739 B 73458 3741 B 75376	3713	В	62316
3716 B 62585 3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3738 B 71249 3739 B 73458 3740 B 75376	3714	В	61722
3717 B 64473 3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3738 B 71249 3739 B 73458 3741 B 75376	3715	В	63603
3718 B 63362 3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3716	В	62585
3719 B 65285 3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3717	В	64473
3720 B 64203 3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3718	В	63362
3721 B 66103 3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3719	В	65285
3722 B 64850 3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73458 3740 B 75376	3720	В	64203
3723 B 66749 3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3721	В	66103
3724 B 64899 3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3722	В	64850
3725 B 66776 3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3723	В	66749
3726 B 65164 3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3724	В	64899
3727 B 67067 3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3725	В	66776
3728 B 67514 3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3726	В	65164
3729 B 69390 3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3727	В	67067
3730 B 69097 3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3728	В	67514
3731 B 71033 3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3729	В	69390
3732 B 69470 3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3730	В	69097
3733 B 71354 3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376		В	71033
3734 B 69961 3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3732	В	69470
3735 B 71898 3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3733	В	71354
3736 B 70707 3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3734	В	69961
3737 B 72579 3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376		В	71898
3738 B 71249 3739 B 73134 3740 B 73458 3741 B 75376	3736	В	70707
3739 B 73134 3740 B 73458 3741 B 75376	3737	В	72579
3740 B 73458 3741 B 75376	3738	В	71249
3741 B 75376	3739	В	73134
	3740	В	73458
3742 B 75121		В	75376
	3742	В	75121

SEQ ID	Or.	position
5304	В	839800
5305	В	841700
5306	В	840808
5307	В	842715
5308	В	841975
5309	В	843834
5310	В	842679
5311	В	844614
5312	В	843342
5313	В	845247
5314	В	843736
5315	В	845626
5316	В	846423
5317	В	848330
5318	В	844423
5319	В	846258
5320	В	848265
5321	В	850174
5322	В	850343
5323	В	852246
5324	В	851875
5325	В	853765
5326	В	853944
5327	В	855822
5328	В	855056
5329	В	856964
5330	В	855750
5331	В	857714
5332	В	856488
5333	В	858370
5334	В	857403
5335	В	859303
5336	В	859659
5337	В	861570

SEQ ID Or. position 2148 F 471590 2149 F 469835 2150 F 473033 2151 F 471133 2152 F 473761 2153 F 471861 2154 F 474383 2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2149 F 469835 2150 F 473033 2151 F 471133 2152 F 473761 2153 F 471861 2154 F 474383 2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2150 F 473033 2151 F 471133 2152 F 473761 2153 F 471861 2154 F 474383 2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2151 F 471133 2152 F 473761 2153 F 471861 2154 F 474383 2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2152 F 473761 2153 F 471861 2154 F 474383 2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2153 F 471861 2154 F 474383 2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2154 F 474383 2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2155 F 472478 2156 F 475333 2157 F 473465 2158 F 476279	
2156 F 475333 2157 F 473465 2158 F 476279	
. 2157 F 473465 2158 F 476279	
2158 F 476279	
2450	
2159 F 474390	
2160 F 478446	
2161 F 476546	
2162 F 478869	
2163 F 476918	
2164 F 479441	
2165 F 477548	
2166 F 479676	
2167 F 477775	
2168 F 481277	
2169 F 479377	
2170 F 481635	
2171 F 479745	
2172 F 483172	
2173 F 481279	
2174 F 484659	
2175 F 482764	
2176 F 485003	
2177 F 483097	
2178 F 487946	
2179 F 486083	
2180 F 487946	
2181 F 486093	

SEQ ID	Or.	position
3743	В	77020
3744	В	75741
3745	В	77608
3746	В	77447
3747	В	79300
3748	В	77535
3749	В	79430
3750	В	78333
3751	В	80243
3752	В	79300
3753	В	81197
3754	В	82201
3755	В	84100
3756	В	83493
3757	В	85405
3758	В	85075
3759	В	86973
3760	В	87141
3761	В	89086
3762	В	88903
3763	В	90810
3764	В	88038
3765	В	89946
3766	В	88981
3767	В	90884
3768	В	89485
3769	В	91385
3770	В	89975
3771	В	91855
3772	В	91680
3773	В	93567
3774	В	92008
3775	В	93902
3776	В	92633

SEQ ID	Or.	position
5338	В	860166
5339	В	862082
5340	В	860879
5341	В	862767
5342	В	861861
5343	В	863727
5344	В	862284
5345	В	864173
5346	В	863792
5347	В	865660
5348	В	864164
5349	В	866050
5350	В	864925
5351	В	866860
5352	В	866468
5353	В	868368
5354	В	866860
5355	В	868734
5356	В	867952
5357	В	869878
5358	В	869311
5359	В	871226
5360	В	869582
5361	В	871517
5362	В	871614
5363	В	873536
5364	В	872804
5365	В	874702
5366	В	873093
5367	В	874980
5368	В	874158
5369	В	876056
5370	В	874033
5371	В	875932

PCT/1B98/01939

SEQ ID	Or.	position
2182	F	489220
2183	F	487274
2184	F	490276
2185	F	488388
2186	F	492138
2187	F	490229
2188	F	492475
2189	F	490618
2190	F	493591
2191	F	491719
2192	F	494297
2193	F	492436
2194	F	494530
2195	F	492679
2196	F	494637
2197	F	492753
2198	F	495467
2199	F	493559
2200	F	496076
2201	F	494126
2202	F	497468
2203	F	495569
2204	F	498050
2205	F	496160
2206	F	498994
2207	F	497096
2208	F	500571
2209	F	498671
2210	F	501547
2211	F	499671
2212	F	502469
2213	F	500572
2214	F	503435
2215	F	501547

SEQ ID	Or.	position
3777	В	94569
3778	В	93390
3779	В	95288
3780	В	94354
3781	В	96254
3782	В	94897
3783	В	96772
3784	В	98519
3785	В	100439
3786	В	98962
3787	В	100853
3788	В	100451
3789	В	102387
3790	В	101639
3791	В	103473
3792	В	102457
3793	В	104357
3794	В	102745
3795	В	104666
3796	В	104544
3797	В	106464
3798	В	105338
3799	В	107237
3800	В	106127
3801	В	108014
. 3802	В	108693
3803	В	110587
3804	В	109189
3805	В	111079
3806	В	109684
3807	В	111580
3808	В	110587
3809	В	112486
3810	В	112740

SEQ ID	Or.	position
5372	В	874670
5373	В	876580
5374	В	875606
5375	В	877506
5376	В	876619
5377	В	878519
5378	В	878160
5379	В	880034
5380	В	878429
5381	В	880292
5382	В	879336
5383	В	881230
5384	В	879393
5385	В	881281
5386	В	880089
5387	В	881994
5388	В	881108
5389	В	883062
5390	В	882094
5391	В	884013
5392	В	883124
5393	В	885027
5394	В	884014
5395	В	885924
5396	В	884530
5397	В	886432
5398	B	885226
5399	В	887139
5400	В	889010
5401	В	890900
5402	В	890421
5403	В	892310
5404	В	891438
5405	В	893287

SEQ ID	Or.	position
2216	F	505469
2217	F	503545
2218	F	506768
2219	F	504880
2220	F	507356
2221	F	505530
2222	F	508015
2223	F	506157
2224	F	508247
2225	F	506351
2226	F	509270
2227	F	507356
2228	F	510759
2229	F	508918
2230	F	511268
2231	F	509359
2232	F	512124
2233	F	510202
2234	F	512836
2235	F	510926
2236	F	514569
2237	F	512663
2238	F	514688
2239	F	512874
2240	F	515334
2241	F	513415
2242	F	515516
2243	F	513670
2244	F	516230
2245	F	514348
2246	F	517181
2247	F	515261
2248	F	517840
2249	F	515977

	-			
SEQ ID	0:	r.	р	osition
3811]	В	1	14673
3812	1	В	1	13684
3813		В	1	15653
3814		В	1	14216
3815		В	ī	.16158
3816	T	В	1	14836
3817	T	В	1	16732
3818	T	В	1	15473
3819	T	В]	17380
. 3820	T	В	13	115898
3821	T	В	1	117797
3822	T	В	1	120031
3823	†	В	1	121926
3824	†	В	1	124231
3825	T	В		126158
3826		В	1	125215
3827	T	В		127115
3828	T	В	1	125352
3829	†	В	1	127271
3830	1	В	1	126492
3831	1	В	1	128390
3832	7	В		127150
3833	1	В	1	129050
3834	1	В		128010
3835	1	В		129905
3836	1	В	-	129947
3837	1	В		131873
3838	1	В		131255
3839	1	В		133205
3840		В		131873
3841		В		133749
3842		В		133381
3843		В		135305
3844		В		133804
			_	

SEQ ID	Or.	position	
5406	В	891703	
5407	В	893606	
5408	В	893606	
5409	В	895490	
5410	В	894049	
5411	В	896024	
5412	В	894139	
5413	В	896074	
5414	В	894545	
5415	·B	896413	
5416	В	894999	
5417	В	896912	
5418	В	896127	
5419	В	898012	
5420	В	897049	
5421	В	898949	
5422	В	901018	
5423	В	902955	
5424	В	902393	
5425	В	904301	
5426	В	904098	
5427	В	906002	
5428	В	903951	
5429	В	905851	
5430	В	905825	
5431	В	907725	
5432	В	906700	
5433	В	908669	
5434	В	907174	
5435	В	909066	
5436	В	907579	
5437	В	909480	
5438	В	908962	
5439	В	910922	

	۹
~~	è

SEQ ID	Or.	position
2250	F	518184
2251	F	516283
2252	F	518704
2253	F	516804
2254	F	519358
2255	F	517404
2256	F	520483
2257	F	518598
2258	F	521632
2259	F	519765
2260	F	521919
2261	F	520024
2262	F	523372
2263	F	521495
2264	F	524404
2265	F	522508
2266	F	525498
2267	F	523600
2268	F	525687
2269	F	523753
2270	F	526036
2271	F	524164
2272	F	526632
2273	F	524732
2274	F	528073
2275	F	526158
2276	F	528835
2277	F	526999
2278	F	529393
2279	F	527504
2280	F	530004
2281	F	528082
2282	F	530518
2283	F	528594

SEQ ID	Or.	position
3845	В	135704
3846	В	134219
3847	В	136133
3848	В	134729
3849	В	136633
3850	В	137694
3851	В	139583
3852	В	140496
3853	В	142396
3854	В	140953
3855	В	142856
3856	В	142031
3857	В	143950
3858	В	143520
3859	В	145425
3860	В	144066
3861	В	145967
3862	В	144629
3863	В	146519
3864	В	146547
3865	В	148446
3866	В	147304
3867	В	149227
3868	В	148296
3869	В	150255
3870	В	148769
3871	В	150670
3872	В	149320
3873	В	151168
3874	В	149532
3875	В	151470
3876	В	149934
3877	В	151845
3878	В	151168

SEQ ID	Or.	position
5440	В	909415
5441	В	911315
5442	В	909804
5443	В	911704
5444	В	910218
5445	В	912075
5446	В	910834
5447	В	912689
5448	В	911225
5449	В	913064
5450	В	912492
5451	В	914381
5452	В	912852
5453	В	914763
5454	В	913438
5455	В	915340
5456	В	913901
5457	В	915814
5458	В	914730
5459	В	916694
5460	В	915356
5461	В	917256
5462	В	915717
5463	В	917608
5464	В	916854
5465	В	918761
5466	В	916762
5467	В	918712
5468	В	917848
5469	В	919756
5470	В	918588
5471	В	920424
5472	В	918875
5473	В	920796

SEQ ID	Or.	position
2284	F	532100
2285	F	530224
2286	F	533025
2287	F	531125
2288	F	533710
2289	F	531825
2290	F	534658
2291	F	532758
2292	F	535737
2293	F	533828
2294	F	539456
2295	F	537568
2296	F	540290
2297	F	538375
2298	F	540672
2299	F	538777
2300	F	541573
2301	F	539706
2302	F	542999
2303	F	541102
2304	F	543922
2305	F	542057
2306	F	544268
2307	F	542354
2308	F	544691
2309	F	542785
2310	F	546323
2311	F	544441
2312	F	546467
2313	F	544650
2314	F	547257
2315	F	545357
2316	F	547658
2317	F	545781

SEQ ID	Or.	position
3879	В	153047
3880	В	152275
3881	В	154165
3882	В	152887
3883	В	154804
3884	В	153600
3885	В	155482
3886	В	154217
3887	В	156157
3888	В	155523
3889	В	157396
3890	В	156823
3891	В	158731
3892	В	157745
3893	В	159645
3894	В	159207
3895	В	161084
3896	В	160216
3897	В	162127
3898	В	161451
3899	В	163350
3900	В	161818
3901	В	163726
3902	В	162601
3903	В	164501
3904	В	163282
3905	В	165205
3906	В	164171
3907	В	166082
3908	В	165812
3909	В	167672
3910	В	166939
3911	В	168861
3912	В	168421

SEQ ID	Or.	position
5474	В	919756
5475	В	921710
5476	В	920055
5477	В	921949
5478	В	920389
5479	В	922328
5480	В	921130
5481	В	922978
5482	В	921517
-5483	В	923414
5484	В	921740
5485	В	923646
5486	В	921979
5487	В	923926
5488	В	922396
5489	В	924327
5490	В	922729
5491	В	924611
5492	В	923256
5493	В	925216
5494	В	923673
5495	В	925589
5496	В	924297
5497	В	926176
5498	В	924645
5499	В	926555
5500	В	925216
5501	В	927117
5502	В	925589
5503	В	927489
5504	В	926980
5505	В	928903
5506	В	927408
5507	В	929331

SEQ ID	Or.	position
2318	F	548406
2319	F	546466
2320	F	549443
2321	F	547527
2322	F	550193
2323	F	548288
2324	F	551554
2325	F	549665
2326	F	552877
2327	F	550963
2328	F	554708
2329	F	552807
2330	F	556293
2331	F	554381
2332	F	557095
2333	F	555164
2334	F	557522
2335	F	555656
2336	F	558021
2337	F	556191
2338	F	558964
2339	F	557076
2340	F	560913
2341	F	559007
2342	F	562832
2343	F	561002
2344	F	563374
2345	F	561474
2346	F	565061
2347	F	563198
2348	F	566840
2349	F	564908
2350	F	567802
2351	F	565896

3913 B 170322 3914 B 169503 3915 B 171369 3916 B 170715 3917 B 172587 3918 B 171554 3919 B 173512 3920 B 172596 3921 B 174496 3922 B 173021 3923 B 174716 3924 B 176619 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 177530 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180239 3935 B 182181 3936 B 182964 3939 B 182864 3939 B 183572 3940 B 184750 <t< th=""><th>SEQ ID</th><th>Or.</th><th>position</th></t<>	SEQ ID	Or.	position
3915 B 171369 3916 B 170715 3917 B 172587 3918 B 171554 3919 B 173512 3920 B 172596 3921 B 174496 3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3939 B 183572 3940 B 184750 3941 B 184750 3942 B 185007 <t< td=""><td>3913</td><td>В</td><td>170322</td></t<>	3913	В	170322
3916 B 170715 3917 B 172587 3918 B 171554 3919 B 173512 3920 B 172596 3921 B 174496 3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3942 B 183876 3943 B 185007 3945 B 186910 <td>3914</td> <td>В</td> <td>169503</td>	3914	В	169503
3917 B 172587 3918 B 171554 3919 B 173512 3920 B 172596 3921 B 174496 3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3941 B 185778 3943 B 185007 3945 B 186910 <td>3915</td> <td>В</td> <td>171369</td>	3915	В	171369
3918 B 171554 3919 B 173512 3920 B 172596 3921 B 174496 3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3916	В	170715
3919 B 173512 3920 B 172596 3921 B 174496 3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180239 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3941 B 184750 3942 B 185007 3945 B 186910	3917	В	172587
3920 B 172596 3921 B 174496 3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3941 B 185778 3943 B 185007 3945 B 186910	3918	В	171554
3921 B 174496 3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3919	В	173512
3922 B 173021 3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 177830 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3920	В	172596
3923 B 174847 3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 177830 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182864 3937 B 182864 3939 B 183572 3940 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3921	В	174496
3924 B 174716 3925 B 176619 3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3922	В	173021
3925 B 176619 3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3923	В	174847
3926 B 175205 3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3924	В	174716
3927 B 177143 3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 182972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185007 3945 B 186910	3925	В	176619
3928 B 175943 3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3926	В	175205
3929 B 177830 3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 186910	3927	В	177143
3930 B 177244 3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3928	В	175943
3931 B 179180 3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3929	В	177830
3932 B 178337 3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3930	В	177244
3933 B 180239 3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3931	В	179180
3934 B 180274 3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3932	В	178337
3935 B 182181 3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3933	В	180239
3936 B 180972 3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3934	В	180274
3937 B 182864 3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910		В	
3938 B 181659 3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910		В	180972
3939 B 183572 3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3937	В	182864
3940 B 182864 3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910		В	181659
3941 B 184750 3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910		В	183572
3942 B 183876 3943 B 185778 3944 B 185007 3945 B 186910	3940	В	182864
3943 B 185778 3944 B 185007 3945 B 186910		В	184750
3944 B 185007 3945 B 186910	3942	В	183876
3945 B 186910		В	185778
		В	185007
3946 B 186246		В	
	3946	В	186246

SEQ ID	Or.	position
5508	В	927824
5509	В	929727
5510	В	928418
5511	В	930287
5512	В	928979
5513	В	930879
5514	В	930474
5515	В	932367
5516	В	930879
5517	В	932776
5518	В	931298
5519	В	933223
5520	В	931886
5521	В	933812
5522	В	932187
5523	В	934117
5524	В	932803
5525	В	934733
5526	В	933421
5527	В	935352
5528	В	933841
5529	В	935758
5530	В	934062
5531	В	935933
5532	В	934794
5533	В	936682
5534	В	936606
5535	В	938521
5536	В	938373
5537	В	940324
5538	В	939321
5539	В	941229
5540	В	941153
5541	В	943053

	26

SEQ ID	Or.	position
2352	F	571045
2353	F	569137
2354	F	572300
2355	F	570362
2356	F	572512
2357	F	570612
2358	F	572627
2359	F	570753
2360	F	573416
2361	F	571539
2362	F	573964
2363	F	572065
2364	F	574221
2365	F	572303
2366	F	574704
2367	F	572781
2368	F	574795
2369	F	572936
2370	F	575229
2371	F	573350
2372	F	576318
2373	F	574384
2374	F	577796
2375	F	575893
2376	F	578774
2377	F	576870
2378	F	581976
2379	F	580073
2380	F	582589
2381	F	580679
2382	F	582962
2383	F	581060
2384	F	583210
2385	F	581316
L	ــــــــــــــــــــــــــــــــــــــ	

SEQ ID	Or.	position
3947	В	188160
3948	В	187080
3949	В	189016
3950	В	187490
3951	В	189421
3952	В	188044
3953	В	189929
3954	В	189711
3955	В	191656
3956	В	190594
3957	В	192533
3958	F	190731
3959	В	192679
3960	В	192027
3961	В	193906
3962	В	192684
3963	В	194643
3964	В	193419
3965	В	195348
3966	В	194878
3967	В	196750
3968	В	195270
3969	В	197166
3970	В	197255
3971	В	199165
3972	В	197859
3973	В	199756
3974	В	198443
3975	В	200328
3976	. B	199202
3977	В	201084
3978	В	200198
3979	В	202084
3980	В	200547

SEQ ID	Or.	position
5542	В	942291
5543	В	944212
5544	В	944964
5545	В	946809
5546	В	945527
5547	В	947426
5548	В	946546
5549	В	948430
5550	В	946896
5551	В	948823
5552	В	948677
5553	В	950581
5554	В	949505
5555	В	951398
5556	В	949834
5557	В	951743
5558	В	950897
5559	В	952796
5560	В	951550
5561	В	953534
5562	В	951870
5563	В	953763
5564	В	953037
5565	В	954930
5566	В	954509
5567	В	956384
5568	В	955397
5569	В	957278
5570	В	958191
5571	В	960060
5572	В	959570
5573	В	961432
5574	В	961273
5575	В	963183

SEQ ID	Or.	position
2386	F	583564
2387	F	581697
2388	F	584048
2389	F	582179
2390	F	584797
2391	F	582897
2392	F	584978
2393	F	583031
2394	F	586256
2395	F	584320
2396	F	587527
2397	F	585631
2398	F	588892
2399	F	587052
2400	F	589362
2401	F	587452
2402	F	590516
2403	F	588616
2404	F	592168
2405	F	590235
2406	F	592629
2407	F	590708
2408	F	592901
2409	F	590973
2410	F	593863
2411	F	591990
2412	F	595416
2413	F	593484
2414	F	595935
2415	F	593962
2416	F	597025
2417	F	595158
2418	F	598254
2419	F	596402

200		
SEQ ID	Or.	position
3981	В	202447
3982	В	200934
3983	В	202806
3984	В	201224
3985	В	203115
3986	В	202606
3987	В	204583
3988	В	203735
3989	В	205603
3990	В	204218
3991	В	206147
3992	В	206686
3993	В	208569
3994	В	207672
3995	В	209558
3996	В	208799
3997	В	210648
3998	В	209701
3999	В	211599
4000	В	210500
4001	В	212364
4002	В	211064
4003	В	212957
4004	В	211557
4005	В	213453
4006	В	213248
4007	В	215101
4008	В	214372
4009	В	216286
4010	В	214931
4011	В	216887
4012	В	215375
4013	В	217268
4014	В	216928

CEO TD	T	T
SEQ ID	Or.	position
5576	В	961837
5577	В	963749
5578	В	962823
5579	В	964695
5580	В	962199
5581	В	964099
5582	В	965286
5583	В	967118
5584	В	965928
5585	В	967828
5586	В	967261
5587	В	969179
5588	В	968345
5589	В	970181
5590	В	969123
5591	В	971023
5592	В	970973
5593	В	972849
5594		972081
5595		973933
5596		973279
5597		975173
5598	L l	974803
5599		976683
5600		975459
5601		977346
5602		976431
5603		978335
5604	В	976740
5605		978640
5606		977175
5607		979042
5608	В	977855
5609	В	979768

SEQ ID	Or.	position
2420	F	600515
2421	F	598575
2422	F	601691
2423	F	599745
2424	F	603291
2425	F	601376
2426	F	603538
2427	F	601638
2428	F	604263
2429	F	602388
2430	F	605359
2431	F	603425
2432	F	606622
2433	F	604721
2434	F	607722
2435	F	605908
2436	F	609039
2437	F	607143
2438	F	609842
2439	F	607958
2440	F	611565
2441	F	609657
2442	F	612719
2443	F	610819
2444	F	613473
2445	F	611565
2446	F	614096
2447	F	612172
2448	F	615072
2449	F	613207
2450	F	615645
2451	F	613745
2452	F	617266
2453	F	615347

SEQ ID	Or.	position
4015	В	218828
4016	В	218137
4017	В	220037
4018	В	217661
4019	В	219561
4020	В	218937
4021	В	220822
4022	В	219229
4023	В	221130
4024	В	220005
4025	В	221868
4026	В	220654
4027	В	222560
4028	В	221294
4029	В	223195
4030	В	221762
4031	В	223673
4032	В	222338
4033	В	224212
4034	В	223510
4035	В	225417
4036	В	224094
4037	В	226033
4038	В	225417
4039	В	227291
4040	В	226033
4041	В	227907
4042	В	225811
4043	В	227671
4044	В	226947
4045	В	228871
4046	В	227523
4047	В	229432
4048	В	227907

SEQ ID	Or.	position
5610	В	978153
5611	В	980060
5612	В	978655
5613	В	980553
5614	В	979204
5615	В	981104
5616	В	979554
5617	В	981465
5618	В	981423
5619	В	983319
5620	В	980363
5621	В	982289
5622	В	982361
5623	В	984236
5624	В	983818
5625	В	985718
5626	В	984720
5627	В	986608
5628	В	985607
5629	В	987553
5630	В	986323
5631	В	988223
5632	В	986925
5633	В	988825
5634	В	987850
5635	В	989749
5636	В	988354
5637	В	990252
5638	В	988474
5639	В	990393
5640	В	989437
5641	В	991305
5642	В	993662
5643	В	995596

SEQ ID	Or.	position
2454	F	618142
2455	F	616242
2456	F	619019
2457	F	617128
2458	F	619637
2459	F	617695
2460	F	620182
2461	F	618257
2462	F	620929
2463	F	619019
2464	F	621446
2465	F	619529
2466	F	622195
2467	F	620292
2468	F	623244
2469	F	621446
2470	F	623834
2471	F	621954
2472	F	625024
2473	F	623208
2474	F	626291
2475	F	624369
2476	F	626724
2477	F	624821
2478	F	627597
2479	F	625703
2480	F	627927
2481	F	626025
2482	F	628712
2483	F	626787
2484	F	629535
2485	F	627685
2486	F	630055
2487	F	628178

SEQ ID	Or.	position
4049	В	229784
4050	В	228692
4051	В	230578
4052	В	230253
4053	В	232157
4054	В	231299
4055	В	233194
4056	В	233226
4057	В	235130
4058	В	234073
4059	В	235950
4060	В	234510
4061	В	236399
4062	В	235094
4063	В	236993
4064	В	236552
4065	В	238440
4066	В	238440
4067	В	240381
4068	В	238989
4069	В	240917
4070	В	240294
4071	В	242181
4072	В	242260
4073	В	244157
4074	В	243066
4075	В	245029
4076	В	244703
4077	В	246603
4078	В	246151
4079	В	248017
4080	В	247104
4081	В	248997
4082	В	248001

		
SEQ ID	Or.	position
5644	В	994015
5645	В	995906
5646	В	994084
5647	В	995955
5648	В	994523
5649	В	996382
5650	В	995903
5651	В	997791
5652	В	996831
5653	В	998764
5654	В	998505
5655	В	1000417
5656	В	999445
5657	В	1001345
5658	В	1001253
5659	В	1003169
5660	В	1001751
5661	В	1003637
5662	В	1001954
5663	В	1003786
5664	В	1004003
5665	В	1005872
5666	В	1005114
5667	В	1006999
5668	В	1005620
5669	В	1007561
5670	В	1007761
5671	В	1009618
5672	В	1008052
5673	В	1009941
5674	В	1008954
5675	В	1010818
5676	В	1009679
5677	В	1011621

SEQ ID	Or.	position
2488	F	630672
2489	F	628789
2490	F	637125
2491	F	635224
2492	F	637807
2493	F	635913
2494	F	639960
2495	F	638102
2496	F	639960
2497	F	638012
2498	F	643252
2499	F	641355
2500	F	644146
2501	F	642204
2502	F	645175
2503	F	643275
2504	F	645519
2505	F	643652
2506	F	646869
2507	F	644983
2508	F	649714
2509	F	647800
2510	F	650199
2511	F	648260
2512	F	651421
2513	F	649536
2514	F	652285
2515	F	650397
2516	F	652562
2517	F	650653
2518	F	659653
2519	F	657741
2520	F	661449
2521	F	659621

SEQ ID	Or.	position
4083	В	249872
4084	В	248835
4085	В	250713
4086	В	249697
4087	В	251574
4088	В	250643
4089	В	252560
4090	В	251439
4091	В	253306
4092	В	252401
4093	В	254231
4094	В	253312
4095	В	255224
4096	В	256969
4097	В	258840
4098	В	258065
4099	В	259964
4100	В	258945
4101	В	260826
4102	В	259428
4103	В	261313
4104	В	261845
4105	В	263746
4106	В	264350
4107	В	266263
4108	В	264963
4109	В	266887
4110	В	265848
4111	В	267749
4112	В	266644
4113	В	268546
4114	В	268188
4115	В	270091
4116	В	268188

SEQ ID	Or.	position
5678	В	1012274
5679	В	1014193
5680	В	1012682
5681	В	1014550
5682	В	1012855
5683	В	1014755
5684	В	1013104
5685	В	1014996
5686	В	1013698
5687	В	1015571
5688	В	1014289
5689	В	1016181
5690	В	1014730
5691	В	1016653
5692	В	1015459
5693	В	1017377
5694	В	1016272
5695	В	1018122
5696	В	1017377
5697	В	1019285
5698	В	1018043
5699	В	1019888
5700	В	1019146
5701	В	1021064
5702	В	1019421
5703	В	1021323
5704	В	1020440
5705	В	1022319
5706	В	1021269
5707	В	1023161
5708	В	1021789
5709	В	1023722
5710	В	1022638
5711	В	1024535

SEQ ID	Or.	position
2522	F	662058
2523	F	660167
2524	F	662726
2525	F	660831
2526	F	663526
2527	F	661591
2528	F	664035
2529	F	662134
2530	F	665504
2531	F	663591
2532	F	665530
2533	F	663663
2534	F	666606
2535	F	664705
2536	F	667901
2537	F	665987
2538	F	667953
2539	F	666037
2540	F	668397
2541	F	666496
2542	F	669235
2543	F	667366
2544	F	669763
2545	F	667879
2546	F	670513
2547	F	668612
2548	F	670963
2549	F	669058
2550	F	672473
2551	F	670573
2552	F	672985
2553	F	671072
2554	F	674381
2555	F	672493

SEQ ID	Or.	position
4117	В	270091
4118	В	268546
4119	В	270440
4120	В	268785
4121	В	270697
4122	В	270439
4123	В	272288
4124	В	271181
4125	В	273043
4126	В	271833
4127	В	273738
4128	В	273188
4129	В	275062
4130	В	273817
4131	В	275718
4132	В	275062
4133	В	277005
4134	В	275886
4135	В	277857
4136	В	277923
4137	В	279868
4138	В	279043
4139	В	281004
4140	В	280126
4141	В	282004
4142	В	281004
4143	В	282911
4144	В	281825
4145	В	283746
4146	В	282335
4147		284236
4148	В	284583
4149		286455
4150	В	285055

SEQ ID	Or.	position
5712	В	1023900
5713	В	1025787
5714	В	1024169
5715	В	1026083
5716	В	1024996
5717	В	1026938
5718	В	1025295
5719	В	1027165
5720	В	1026136
5721	В	1028031
5722	В	1026823
5723	E	1028699
5724	В	1027642
5725	В	1029524
5726	В	1030824
5727	В	1032737
5728	В	1033510
5729	В	1035372
5730	В	1032306
5731	В	1034209
5732	В	1037275
5733	В	1162
5734	В	1036130
5735	В	1038037
5736	В	1036727
5737	B 	149
5738	В	225
5739	В	2104
5740	В	17209
5741	В	19109
5742	В	32032
5743	В	33899
5744	В	57057
5745	В	58954

ar 2 ==		
SEQ ID	Or.	position
2556	F	675029
2557	F	673135
2558	F	676254
2559	F	674357
2560	F	677481
2561	F	675559
2562	F	678423
2563	F	676580
2564	F	679049
2565	F	677156
2566	F	680360
2567	F	678423
2568	F	681257
2569	F	679420
2570	F	682281
2571	F	680435
2572	F	682870
2573	F	681012
2574	F	684147
2575	F	682281
2576	F	684582
2577	F	682664
2578	F	685978
2579	F	684033
2580	F	687121
2581	F	685186
2582	F	687974
2583	F	686044
2584	F	688169
2585	F	686313
2586	F	689393
2587	F	687511
2588	F	689580
2589	F	687727

SEQ ID	Or.	position
4151	В	286921
4152	В	285894
4153	В	287794
4154	В	286441
4155	В	288315
4156	В	286921
4157	В	288811
4158	В	288145
4159	В	290018
4160	В	289448
4161	В	291407
4162	В	290899
4163	В	292805
4164	В	291814
4165	В	293655
4166	В	292489
4167	В	294373
4168	В	293317
4169	В	295183
4170	В	295073
4171	В	297037
4172	В	295932
4173	В	297846
4174	В	296556
4175	В	298475
4176	В	297474
4177	В	299413
4178	В	298970
4179	В	300855
4180	В	300679
4181	В	302595
4182	В	302372
4183	В	304272
4184	В	305137

SEQ ID	Or.	position
5746	В	57141
5747	В	59033
5748	В	65406
5749	В	67210
5750	В	73871
5751	В	75741
5752	В	78956
5753	В	80903
5754	В	80042
5755	В	81944
5756	В	82642
5757	В	84491
5758	В	87820
5759	В	89658
5760	В	110184
5761	В	112086
5762	В	111873
5763	В	113837
5764	В	112302
5765	В	114206
5766	В	113165
5767	В	115093
5768	В	114270
5769	В	116158
5770	В	121039
5771	В	122904
5772	В	125742
5773	В	127643
5774	В	132170
5775	В	134028
5776	В	144647
5777	В	146547
5778	В	150960
5779	В	152837

PCT/IB98/01939

SEQ ID	Or.	position
2590	F	690204
2591	F	688342
2592	F	690431
2593	F	688497
2594	F	691790
2595	F	689919
2596	F	693614
2597	F	691704
2598	F	694723
2599	F	692821
2600	F	696922
2601	F	695033
2602	F	697714
2603	F	695816
2604	F	698510
2605	F	696612
2606	F	700037
2607	F	698119
2608	F	700691
2609	F	698783
2610	F	701885
2611	F	699984
2612	F	703303
2613	F	701403
2614	F	704791
2615	F	702877
2616	F	705452
2617	F	703584
2618	F	705918
2619	F	704019
2620	F	706241
2621	F	704322
2622	F	707833
2623	F	705939

	T	· · · · · · · · · · · · · · · · · · ·
SEQ ID	Or.	position
4185	В	307039
4186	В	306377
4187	В	308287
4188	В	306730
4189	В	308614
4190	В	307199
4191	В	309120
4192	В	309018
4193	В	310903
4194	В	310128
4195	В	312001
4196	В	310966
4197	В	312899
4198	В	311790
4199	В	313705
4200	В	312671
4201	В	314590
4202	В	314590
4203	В	316484
4204	В	314977
4205	В	316880
4206	В	315775
4207	В	317646
4208	В	316760
4209	В	318627
4210	В	317541
4211	В	319422
4212	В	317829
4213	В	319763
4214	В	318703
4215	В	320628
4216	В	318094
4217	В	320048
4218	В	319182

SEQ ID	Or.	position
5780	В	164761
5781	В	166686
5782	В	166362
5783	В	168305
5784	В	168970
5785	В	170889
5786	В	171056
5787	В	173021
5788	В	177747
5789	В	179629
5790	В	188605
5791	В	190552
5792	В	189016
5793	В	190924
5794	В	190871
5795	В	192749
5796	В	197533
5797	В	199449
5798	В	211604
5799	В	213554
5800	В	235455
5801	В	237385
5802	В	237448
5803	В	239387
5804	В	250266
5805	В	252155
5806	В	253731
5807	В	255663
5808	В	255115
5809	В	256969
5810	В	272158
5811	В	274093
5812	В	276317
5813	В	278190

SEQ ID	Or.	position
2624	F	708029
2625	F	706086
2626	F	708653
2627	F	706753
2628	F	710042
2629	F	708142
2630	F	711185
2631	F	709291
2632	F	712521
2633	F	710641
2634	F	713432
2635	F	711506
2636	F	713901
2637	F	711987
2638	F	714557
2639	F	712708
2640	F	715339
2641	F	713437
2642	F	715702
2643	F	713761
2644	F	716892
2645	F	714970
2646	F	718240
2647	F	716381
2648	F	718240
2649	F	716380
2650	F	719563
2651	F	717658
2652	F	719916
2653	F	718025
2654	F	720346
2655	F	718429
2656	F	721306
2657	F	719440

SEQ ID	Or.	position
4219	В	321067
4220	В	320404
4221	В	322278
4222	В	321720
4223	В	323625
4224	В	322158
4225	В	324071
4226	В	322582
4227	В	324500
4228	В	323371
4229	В	325260
4230	В	325173
4231	В	327057
4232	В	325882
4233	В	327770
4234	В	326509
4235	В	328388
4236	В	327463
4237	В	329330
4238	В	328374
4239	В	330270
4240	В	328850
4241	В	330751
4242	В	329330
4243	В	331210
4244	В	329883
4245	В	331822
4246	В	330886
4247	В	332797
4248	В	331395
4249	В	333375
4250	В	331990
4251	В	333884
4252	В	332669

SEQ ID	Or.	position
5814	В	278470
5815	В	280366
5816	В	283005
5817	В	284873
5818	В	293718
5819	В	295643
5820	В	303690
5821	В	305624
5822	В	309538
5823	В	311476
5824	В	312791
5825	В	314685
5826	В	313073
5827	В	314977
5828	В	313506
5829	В	315343
5830	В	320823
5831	В	322730
5832	В	340723
5833	В	342638
5834	В	353562
5835	В	355444
5836	В	373944
5837	В	375838
5838	В	377997
5839	В	379877
5840	В	379877
5841	В	381778
5842	В	395318
5843	В	397228
5844	В	401846
5845	В	403782
5846	В	410759
5847	В	412677

SEQ ID	Or.	position
2658	F	722178
2659	F	720271
2660	F	723159
2661	F	721259
2662	F	724357
2663	F	722451
2664	F	725491
2665	F	723647
2666	F	726312
2667	F	724417
2668	F	726526
2669	F	724590
2670	F	727245
2671	F	725325
2672	F	728081
2673	F	726209
2674	F	728510
2675	F	726618
2676	F	729214
2677	F	727319
2678	F	733006
2679	F	731064
2680	F	734566
2681	F	732618
2682	F	735410
2683	F	733522
2684	F	736226
2685	F	734388
2686	F	736969
2687	F	735092
2688	F	737678
2689	F	735820
2690	F	738618
2691	F	736719

SEQ ID	Or.	position
4253	В	334575
4254	В	333375
4255	В	335166
4256	В	333811
4257	В	335709
4258	В	334579
4259	В	336497
4260	В	334590
4261	В	336497
4262	В	335362
4263	В	337262
4264	В	335863
4265	В	337723
4266	В	335939
4267	В	337848
4268	В	336558
4269	В	338461
4270	В	337647
4271	В	339503
4272	В	340181
4273	В	342110
4274	В	342069
4275	В	343977
4276	В	342269
4277	В	344168
4278	В	342694
4279	В	344593
4280	В	343594
4281	В	345503
4282	В	344269
4283	В	346199
4284	В	344452
4285	В	346382
4286	В	345362

		· · · · · · · · · · · · · · · · · · ·
SEQ ID	Or.	position
5848	В	411878
5849	В	413779
5850	В	415199
5851	В	417099
5852	В	423479
5853	В	425332
5854	В	428421
5855	В	430332
5856	В	429678
5857	В	431571
5858	В	443036
5859	В	444947
5860	В	444280
5861	В	446161
5862	В	443964
5863	В	445811
5864	В	446392
5865	В	448276
5866	В	468498
5867	В	470382
5868	В	472328
5869	В	474285
5870	В	488594
5871	В	490459
5872	В	497914
5873	В	499837
5874	В	500718
5875	В	502596
5876	В	509811
5877	В	511702
5878	В	511485
5879	В	513385
5880	В	527090
5881	В	529014

SEQ ID	Or.	position
2692	F	739841
2693	F	737941
2694	F	741797
2695	F	739895
2696	F	742583
2697	F	740705
2698	F	743087
2699	F	741169
2700	F	744211
2701	F	742277
2702	F	744391
2703	F	742492
2704	F	744739
2705	F	742813
2706	F	745342
2707	F	743438
2708	F	746197
2709	F	744273
2710	F	746725
2711	F	744784
2712	F	748041
2713	F	746142
2714	F	748723
2715	F	746795
2716	F	749171
2717	F	747310
2718	F	749475
2719	F	747568
2720	F	749761
2721	F	747855
2722	F	752284
2723	F	750384
2724	F	753397
2725	F	751497

SEQ ID	Or.	position
4287	В	347262
4288	В	346199
4289	В	348069
4290	В	347326
4291	В	349228
4292	В	348165
4293	В	350060
4294	В	350399
4295	В	352288
4296	В	351503
4297	В	353403
4298	В	352460
4299	В	354356
4300	В	352948
4301	В	354901
4302	В	353959
4303	В	355890
4304	В	354438
4305	В	356378
4306	В	354997
4307	В	356866
4308	В	356897
4309	В	358793
4310	В	357643
4311	В	359499
4312	В	358323
4313	В	360222
4314	В	360972
4315	В	362863
4316	В	361348
4317	В	363263
4318	В	362109
4319	В	364008
4320	В	362983

SEQ	ID	Or.	position
588	2	В	532083
588	3	В	533999
588	4	В	557487
588	5	В	559357
588	36	В	565191
588	37	В	567099
588	38	В	567452
588	39	В	569355
589	90	В	571110
589	91	В	573047
589	92	В	571557
589	93	В	573461
589	94	В	576288
589	95	В	578181
58	96	В	590890
58	97	В	592770
58	98	В	598813
58	99	В	600714
59	00	В	607146
59	01	В	609012
59	02	В	608260
59	03	В	610162
59	04	В	610621
59	05	В	612514
59	06	В	633573
59	07	В	635473
59	08	В	637702
59	09	В	639603
59	10	В	650757
59	11	В	652667
59	12	В	652808
59	13	В	654682
59	14	В	655545
59	15	В	657446
			_ <u></u>

SEQ ID	Or.	position
2726	F	754693
2727	F	752818
2728	F	756537
2729	F	754648
2730	F	758227
2731	F	756276
2732	F	759119
2733	F	757196
2734	F	759639
2735	F	757745
2736	F	759957
2737	F	758069
2738	F	760675
2739	F	758798
2740	F	761489
2741	F	759589
2742	F	762033
2743	F	760133
2744	F	763116
2745	F	761215
2746	F	764209
2747	F	762315
2748	F	764602
2749	F	762702
2750	F	765834
2751	F	763904
2752	F	766671
2753	F	764806
2754	F	768033
2755	F	766063
2756	F	768572
2757	F	766671
2758	F	769873
2759	F	768006

SEQ ID	Or.	position
4321	В	364867
4322	В	364110
4323	В	366002
4324	В	365415
4325	В	367338
4326	В	365807
4327	В	367733
4328	В	367607
4329	В	369440
4330	В	368881
4331	В	370788
4332	В	369317
4333	В	371209
4334	В	370522
4335	В	372440
4336	В	371311
4337	В	373206
4338	В	373097
4339	В	374941
4340	В	373753
4341	В	375649
4342	В	374424
4343	В	376324
4344	В	374956
4345	В	376888
4346	В	376611
4347	В	378511
4348	В	377297
4349	В	379209
4350	В	378960
4351	В	380880
4352	В	379309
4353	В	381180
4354	В	379667

	1 -	r
SEQ ID	Or.	position
5916	В	661392
5917	В	663292
5918	В	677837
5919	В	679716
5920	В	679748
5921	В	681674
5922	В	732909
5923	В	734756
5924	В	742639
5925	В	744503
5926	В	759613
5927	В	761510
5928	В	760782
5929	В	762671
5930	В	771617
5931	В	773519
5932	В	772628
5933	В	774528
5934	В	788703
5935	В	790577
5936	В	816591
5937	В	818443
5938	В	847145
5939	В	849042
5940	В	868276
5941	В	870177
5942	В	875887
5943	В	877779
5944	В	877137
5945	В	879035
5946	В	884780
5947	В	886680
5948	В	892172
5949	В	894073

WO 33120413			
SEQ ID	Or.	position	
2760	F	769966	
2761	F	768060	
2762	F	770411	
2763	F	768455	
2764	F	771103	
2765	F	769211	
2766	F	771980	
2767	F	770116	
2768	F	773176	
2769	F	771305	
2770	F	773937	
2771	F	771980	
2772	F	776399	
2773	F	774514	
2774	F	776672	
2775	F	774773	
2776	F	777446	
2777	F	775596	
2778	F	779102	
2779	F	777192	
2780	F	781078	
2781	F	779148	
2782	F	782192	
2783	F	780236	
2784	F	785250	
2785	F	783413	
2786	F	785324	
2787	F	783427	
2788	F	786392	
2789	F	784488	
2790	F	787401	
2791	F	785488	
2792	F	787693	

SEQ ID	Or.	position
4355	В	381553
4356	В	380238
4357	В	382152
4358	В	381699
4359	В	383615
4360	В	382790
4361	В	384687
4362	В	383935
4363	В	385837
4364	В	384167
4365	В	386065
4366	В	385479
4367	В	387365
4368	В	385730
4369	В	387635
4370	В	387115
4371	В	389019
4372	В	386903
4373	В	388753
4374	В	387595
4375	В	389504
4376	В	388133
4377	В	390055
4378	В	388524
4379	В	390455
4380	В	389428
4381	В	391321
4382	В	390313
4383	В	392241
4384	В	391321
4385	В	393147
4386	В	392032
4387	В	393943

SEQ ID	Or.	position
5950	В	900990
5951	В	902955
5952	В	902780
5953	В	904687
5954	В	908266
5955	В	910218
5956	В	912811
5957	В	914730
5958	В	935988
5959	В	937863
5960	В	947227
5961	В	949089
5962	В	953426
5963	В	955397
5964	В	966421
5965	В	968345
5966	В	969548
5967	В	971477
5968	В	971390
5969	В	973279
5970	В	972661
5971	В	974581
5972	В	973730
5973	В	975665
5974	В	998885
5975	В	1000774
5976	В	1004572
5977	В	1006449
5978	В	1010507
5979	В	1012353
5980	В	1029707
5981	В	1031628

Publications Cited in the Specification

Adames et al., 1985, Nature, 318:533-538.

Altschul et al., 1993, Nature Genetics, 3:266-272.

Altschul et al., 1997, Nucl. Acids Res., 25:3389-3402.

Altschul, S.F. et al., 1990, J. Mol. Biol., 215:403-410.

Ansubel et al., 1989, Current Protocols in Molecular

Biology, Green Publishing Associates and Wiley Interscience, NY.

Arlinghaus, H.F. et al., 1997, Anal. Biochem., 69, 18, 3747-53.

Bai, M. Et al., 1993, J. Virol., 67:5198-5205.

Barany, F., 1911, Proc. Natl. Acad. Sci. USA, 88:189-193.

Beattie, K. et al., 1993, Clin. Chem., 39(4):719-721.

Bernoist and Chambon, 1981, Nature, 290:304-310.

Borman, S., 1996, Chem. Eng. News, 74(50):42-43.

Brinster et al., 1982, Nature, 296:39-42.

Buckholz, R.G., 1993, Curr. Op. Biotechnology, 4:538-542.

Burg, J.L. et al., 1996, Mol. and Cell. Probes, 10:257-271.

Casas-Ciria J. et al., 1996

Chatelier, R.C. et al., 1995, Anal. Biochem., 229, 1, 112-118.

Chee, M. et al., 1996, Science, 274:610-613.

Chu, B.C.F. et al., 1986, Nucleic Acids Research, 14:5591-5603.

Cole et al., 1985, in Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc., pp. 77-96.

Cote et al., 1983, PNAS USA, 80:2026-2030.

Cserzo, M., Wallin, E., Simon, I. von Heijne G and Elofsson, A., 1997, Prot. Eng., 10:673-676.

DeBoer et al., 1980, Scientific American, 242:74-94.

DeBoer et al., 1983, PNAS USA, 80:21-25.

Derisi, J. et al., 1996, Nature Genet., 14:457-460.

Duck, P. et al., 1990, Biotechniques, 9:142-147.

Edwards, C.P., and Aruffo, A., 1993, Curr. Op. Biotechnology 4:558-563.

Erlich, H.A., 1989, In PCR Technology. Principles and

Applications for DNA Amplification. New York: Stockton Press.

Fanger and Drakeman, 1995, Drug News and Perspectives, 8:133-137.

Felgner, et al., 1987, Proc. Natl. Acad. Sci. USA, 84:7413.

Fodor, S.P.A. et al., 1991, Science, 251:767-771.

Fox, G. Et al., 1989, J. Gen. Virol., 70:625-637.

Fraley et al., 1980, J. Biol. Chem., 255:10431.

Gardner et al., 1981, Nucl. Acids Res. 9:2871.

Gonnet et al., Science, 256:1443-1445.

Grosschedl et al., 1984, Cell, 38:647-658.

Guateli, J.C. et al., 1990, Proc. Natl. Acad. Sci. USA, 87:1874-1878.

Hackstadt T., Trends Microbiol. 1996 5:288-293.

Hammer et al., 1987, Science, 235:53-58.

Hanahan, 1985, Nature, 315:115-122.

Hayashi, S. and Wu, H.C., 1992, in N.M. Hooper and A.J. Turner (ed.) Lipid Modification of Proteins:

A Practical Approach. Oxford University Press, New York, pp. 261-285.

Heinkoff and Heinkoff, 1993, Proteins, 17:49-61.

Herrera-Estrella et al., 1983, Nature, 303:209-213.

Herrera-Estrella, 1984, Nature, 310:115-120.

Higgins et al., 1996, Meth. Enzymol., 266:383-402.

Houbenweyl, 1974, in Meuthode der Organischen Chemie, E. Wunsch Ed., Volume 15-I et 15-II,

Thieme, Stuttgart.

Hsia, R. et al., 1997, Molecular Micorbiology, 25:351-359.

Hueck, C.J., 1998, Molec. Biology Rev., 62:379-433.

Huovinen, P. et al., 1989 Ann., Intern Med 110:612-616.

Huse et al., 1989, Science, 246:1275-1281.

Huygen, K. et al., 1996, Nature Medicine, 2(8):893-898.

Innis, M.A. et al. 1990, in PCR Protocols. A guide to Methods and Applications. San Diego: Academic Press.

Inoue et al., 1987, Nucl. Acids Res., 15:6131-6148.

Inoue et al., 1987, FEBS Lett. 215:327-330.

Kabat E. Et al., 1983, Sequences of Proteins of Immunological Interest, U.S. Dept. Of Health and Human Services.

Kaneda, et al., 1989, Science, 243:375.

Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA, 87:2267-2268.

Kelsey et al., 1987, Genes and Devel., 1:161-171.

Kievitis, T. et al., 1991, J. Virol. Methods, 35:273-286.

Kohler, G. et al., 1975, Nature, 256(5517):495-497.

Kollias et al., 1986, Cell, 46:89-94.

Kozbor et al., 1983, Immunol. Today, 4:72.

Krumlauf et al., 1985, Mol. Cell. Biol., 5:1639-1648.

Krone, J.R. et al., 1997, Anal. Biochem., 244, 1, 124-132.

Kwoh, D.Y. et al., 1989, Proc. Natl. Acad. Sci. USA, 86:1173-1177.

Leder et al., 1986, Cell, 45:485-495.

Lee, C.A., 1997, Trends Microbiol., 5:148-156.

Leininger, E. et al., 1991, PNAS USA, 88:345-349.

Lipshutz, R.J. et al., 1995, Biotechniques, 19(3):442-447.

Livache, T. et al., 1994, Nucleic Acids Research, 22(15):2915-2921.

Lockhart, D.J. et al., 1996, Nature Biotechnol., 14:1675-1680.

Longbottom et al., 1998, Infect Immunol., 66:1317-1324.

Luckow, V.A., 1993, Curr. Op. Biotechnology, 4:564-572.

Lukacova, M. Et al., 1994, Infect. Immunol. June, 62(6):2270-2276.

Mason et al., 1986, Science, 234:1372-1378.

Matson, R.S. et al., 1994, Anal. Biochem., 217:306-310.

Matthews, J.A. et al., 1988, Anal. Biochem., 169:1-25.

Mérel, P., 1994, Biofutur, 139:58.

Merrifield, R.D., 1966, J. Am. Chem. Soc., 88(21):5051-5052.

Midoux, 1993, Nucleic Acids Research, 21:871-878.

Miele, E.A. et al., 1983, J. Mol. Biol., 171:281-295.

Mogram et al., 1985, Nature, 315:338-340.

Morrison et al., 1984, PNAS USA, 81:6851-6855.

Morrison, R.P. et al., 1995. Gene Knockout Mice Establish a Primary Protective Role for Major Histocompatibility Complex Class II-Restricted Responses in Chlamydia trachomatis. Infect. Immun.

63:4661-4668.

Nakai, K. and Kanehisa, M., 1991, Proteins, 11:95-110.

Nielsen, H. et al., 1997, Protein Engin., 10:1-6.

Neuberger et al., 1984, Nature, 312:604-608.

O'Donell-Maloney, M.J., 1996, Trends Biotechnol., 14:401-407.

Olins, P.O., and Lee, S.C., 1993, Recent advances in heterologous gene expression in E. coli. Curr. Op. Biotechnology 4:520-525.

Ornitz et al., 1986, Cold Spring Harbor Symp. Quant. Biol., 50: 399-409.

Pagano et al., 1967, J. Virol., 1:891.

Pearson and Lipman, 1988, PNAS USA, 85(8):2444-2448.

Peterson, E. et al., 1988. Protective Role of Magnesium in the Neutralization by Antibodies of *Chlamydia trachomatis* Infectivity.

Pierschbacher and Ruoslahti, 1987, J. Biol. Chem., 262:17294-17298.

Pinkert et al., 1987, Genes and Devel., 1:268-276.

Pugsley, A.P., 1993, Microbiol. Rev., 57:50-108.

Raulston JE., Mol Microbiol 1995 15:607-616.

Rank, R.G. et al., 1988. Susceptibility to reinfection after a primary chlamydial genital infection. Infect. Immun. 56:2243-2249.

- WO 99/28475 278

Readhead et al., 1987, Cell, 48:703-712.

Reeves, P.R. et al., 1996, in Bacterial Polysaccharide Synthesis and Gene Nomenclature, Elsevier Science Ltd., pp. 10071-10078.

Relman, D. et al., 1990, Cell, 61:1375-1382.

Roivainen, M. Et al., 1994, Virology, 203:357-365.

Rolfs, A. et al., 1991, In PCR Topics. Usage of Polymerase Chain reaction in Genetic and Infectious Disease. Berlin: Springer-Verlag.

Sambrook, J. et al., 1989, In Molecular cloning: A Laboratory Manual. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.

Sanchez-Pescador, R., 1988, J. Clin. Microbiol., 26(10):1934-1938.

Salzberg et al., 1998, Nucl. Acids Res., 26:544-548.

Sani, 1985, Nature, 314:283-286.

Sarver et al., 1990, Science, 247:1222-1225.

Schachter, J. 1980. Chlamydiae, p.357-365. In E.H. Lennette (ed.), Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.

Schnaitman, C.A. and Klena, J.D., 1993, Microbiol. Rev., 57:655-682.

Schneewind, O. Et al., 1995, Science, 268:103-106.

Schwartz and Dayhoff, eds., 1978, Matrices for Detecting

Distance Relationships: Atlas of Protein Sequence and Structure, Washington: National Biomedical Research Foundation.

Segev D., 1992, in ? Non-radioactive Labeling and Detection of Biomolecules ?. Kessler C. Springer Verlag, Berlin, New-York:197-205.

Sheldon, E.L., 1993, Clin. Chem., 39(4):718-719.

Shiver, J.W., 1995, in Vaccines, eds Chanock, R.M. Brown, F. Ginsberg, H.S. & Norrby, E., pp.95-98, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.

Shoemaker, D.D. et al., 1996, Nature Genet., 14:450-456.

Sosnowsky et al., 1997, Proc. Natl. Acad. Sci. USA, 94, 1119-1123.

Struyve, M. et al., 1991, J. Mol. Biol., 218:141-148.

Sundelof, et al., 1993, Scand. J. Infec. Dis., 25:259-261.

Sutcliffe, I.C. and Russell, R.R.B., 1995, J. Bacteriol.

177:1123- 1128.

Swift et al., 1984, Cell, 38:639-646.

Takeda et al., 1985, Nature, 314:452-454.

Tascon, R.E et al., 1996, Nature Medicine, 2(8):888-892.

Thompson et al., 1994, Nucl. Acids Res., 22(2):4673-4680.

Urdea, M.S., 1988, Nucleic Acids Research, 11:4937-4957.

Villa-Kamaroff et al., 1978, PNAS USA, 75:3727-3731.

Wagner et al., 1981, PNAS USA, 78:1441-1445.

Walker, G.T. et al., 1992, Nucleic Acids Research, 20:1691-1696.

Walker, G.T. et al., 1992, Proc. Natl. Acad. Sci. USA, 89:392-396.

White, B.A. et al., 1997, Methods in Molecular Biology, 67, Humana Press, Towota.

Yamamoto et al., 1980, Cell, 22:787-797.

Yershov, G. et al., 1996, Proc. Natl. Acad. Sci. USA, 93:4913-4918.

WHAT IS CLAIMED IS:

- 1. An isolated polynucleotide having a nucleotide sequence of a *Chlamydia* trachomatis genome, comprising
 - (a) the nucleotide sequence of SEQ ID No. 1;
 - (b) the nucleotide sequence contained within the *Chlamydia trachomatis* genomic DNA in ECACC Deposit No. 98112618;
 - (c) the nucleotide sequence contained in a clone insert in ECACC Deposit No. 98112617:
 - (d) a nucleotide sequence exhibiting at least 99.9% identity with the sequence of SEQ ID No. 1; or
 - (e) a nucleotide sequence exhibiting at least 80% homology to SEQ ID No. 1.
- 2. An isolated polynucleotide which hybridizes to SEQ ID No. 1 or to the Chlamydia trachomatis genomic DNA contained in ECACC Deposit No. 98112618 or to a clone insert in ECACC Deposit No. 98112617 under conditions of high stringency.
- 3. An isolated polynucleotide which hybridizes to SEQ ID No. 1 or to the Chlamydia trachomatis genomic DNA contained in ECACC Deposit No. 98112618 under conditions of intermediate stringency.
- 4. An isolated polynucleotide having a nucleotide sequence of an open reading frame (ORF) of a *Chlamydia trachomatis* genome, comprising:
 - (a) a nucleotide sequence chosen from one of ORF2 to ORF 1197;
 - (b) a nucleotide sequence exhibiting at least 99.9% identity with one of ORF2 to ORF 1197; or
 - (c) a nucleotide sequence exhibiting at least 80% homology to one of ORF2 to ORF 1197.
- 5. An isolated polynucleotide which hybridizes to one of ORF2 to ORF 1197 under conditions of high stringency.
- 6. An isolated polynucleotide which hybridizes to one of ORF2 to ORF 1197 under conditions of intermediate stringency.
- 7. The polynucleotide of Claim 2, 3, 4, 5, or 6 which encodes the following polypeptides or fragments thereof:

- (a) a Chlamydia trachomatis transmembrane polypeptide having between 1 and 3 transmembrane domains;
- (b) a *Chlamydia trachomatis* transmembrane polypeptide having between 4 and 6 transmembrane domains;
- (c) a *Chlamydia trachomatis* transmembrane polypeptide having at least 7 transmembrane domains;
- a Chlamydia trachomatis polypeptide involved in intermediate metabolism of sugars and/or cofactors;
- (e) a Chlamydia trachomatis polypeptide involved in intermediate metabolism of nucleotides or nucleic acids;
- (f) a Chlamydia trachomatis polypeptide involved in metabolism of amino acids or polypeptides;
- a Chlamydia trachomatis polypeptide having involved in metabolism of fatty acids;
- (h) a Chlamydia trachomatis polypeptide involved in the synthesis of the cell wall;
- a Chlamydia trachomatis polypeptide involved in transcription, translation, and/or maturation process;
- (j) a Chlamydia trachomatis transport polypeptide;
- (k) a Chlamydia trachomatis polypeptide involved in the virulence process;
- a Chlamydia trachomatis polypeptide involved in the secretory system and/or which is secreted;
- a Chlamydia trachomatis polypeptide of the cellular envelope or outer cellular envelope of Chlamydia trachomatis.
- (n) a Chlamydia trachomatis surface exposed polypeptide;
- (o) a Chlamydia trachomatis lipoprotein;
- a Chlamydia trachomatis polypeptide involved in lipopolysaccharide biosynthesis;
- (q) a Chlamydia trachomatis KDO-related polypeptide;
- (r) a Chlamydia trachomatis phosphomannomutase-related polypeptide;
- (s) a Chlamydia trachomatis phosphoglucomutase-related polypeptide;
- (t) a Chlamydia trachomatis lipid A component-related polypeptide;
- (u) a Chlamydia trachomatis polypeptide that contains an RGD sequence;
- (v) a Chlamydia trachomatis Type III secreted polypeptide;
- (w) a Chlamydia trachomatis cell wall anchored surface polypeptide; or
- (x) a Chlamydia trachomatis polypeptide that is not found in Chlamydia trachomatis.

- 8. A polynucleotide encoding a fusion protein, comprising one of ORF2 to ORF 1197 of Claim 4, 5, or 6 ligated in frame to a polynucleotide encoding a heterologous polypeptide.
- 9. A recombinant vector that contains the polynucleotide of Claim 1, 2, 3, 4, 5 or 6.
 - 10. A recombinant vector that contains the polynucleotide of Claim 8.
- 11. A recombinant vector that contains the polynucleotide of Claim 4, 5 or 6, operatively associated with a regulatory sequence that controls gene expression.
- 12. A recombinant vector that contains the polynucleotide of Claim 8 operatively associated with a regulatory sequence that controls gene expression.
- 13. A genetically engineered host cell that contains the polynucleotide of Claim 1, 2, 3, 4, 5 or 6.
 - 14. A genetically engineered host cell that contains the polynucleotide of Claim 8.
- 15. A genetically engineered host cell that contains the polynucleotide of Claim 4, 5 or 6 operatively associated with a regulatory sequence that controls gene expression in the host cell.
- 16. A genetically engineered host cell that contains the polynucleotide of Claim 8 operatively associated with a regulatory sequence that controls gene expression in the host cell.
 - 17. A method for producing a polypeptide, comprising:
 - (a) culturing the genetically engineered host cell of Claim 15 under conditions suitable to produce the polypeptide encoded by the polynucleotide; and
 - (b) recovering the polypeptide from the culture.
 - 18. A method for producing a fusion protein, comprising:
 - (a) culturing the genetically engineered host cell of Claim 16 under conditions suitable to produce the fusion protein encoded by the polynucleotide; and
 - (b) recovering the fusion protein from the culture.
 - 19. A polypeptide encoded by the polynucleotide of Claim 4, 5 or 6.

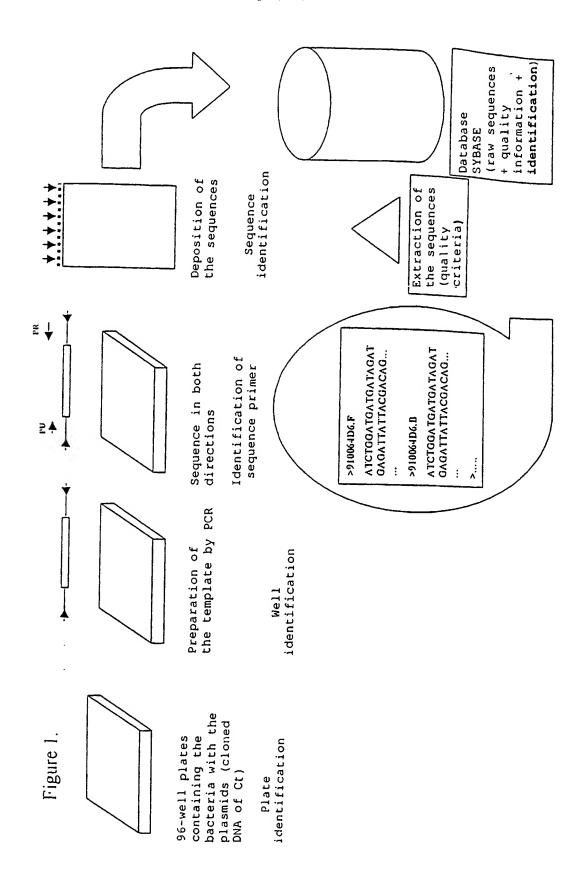
- 20. The polypeptide of Claim 19 which immunoreacts with seropositive serum of an individual infected with *Chlamydia trachomatis*.
- 21. The polypeptide of Claim 19 which comprises the following polypeptides or fragments thereof:
 - (a) a *Chlamydia trachomatis* transmembrane polypeptide having between 1 and 3 transmembrane domains;
 - (b) a *Chlamydia trachomatis* transmembrane polypeptide having between 4 and 6 transmembrane domains;
 - (c) a *Chlamydia trachomatis* transmembrane polypeptide having at least 7 transmembrane domains;
 - (d) a *Chlamydia trachomatis* polypeptide involved in intermediate metabolism of sugars and/or cofactors;
 - (e) a *Chlamydia trachomatis* polypeptide involved in intermediate metabolism of nucleotides or nucleic acids;
 - (f) a *Chlamydia trachomatis* polypeptide involved in metabolism of amino acids or polypeptides;
 - (g) a Chlamydia trachomatis polypeptide involved in metabolism of fatty acids;
 - (h) a Chlamydia trachomatis polypeptide involved in the synthesis of the cell wall;
 - (i) a *Chlamydia trachomatis* polypeptide involved in transcription, translation, and/or maturation process;
 - (j) a Chlamydia trachomatis transport polypeptide;
 - (k) a Chlamydia trachomatis polypeptide involved in the virulence process;
 - a Chlamydia trachomatis polypeptide involved in the secretory system and/or which is secreted;
 - (m) a Chlamydia trachomatis polypeptide of the cellular envelope or outer cellular envelope of Chlamydia trachomatis.
 - (n) a Chlamydia trachomatis surface exposed polypeptide;
 - (o) a Chlamydia trachomatis lipoprotein;
 - (p) a *Chlamydia trachomatis* polypeptide involved in lipopolysaccharide biosynthesis;
 - (q) a Chlamydia trachomatis KDO-related polypeptide;
 - (r) a Chlamydia trachomatis phosphomannomutase-related polypeptide;
 - (s) a Chlamydia trachomatis phosphoglucomutase-related polypeptide;
 - (t) a Chlamydia trachomatis lipid A component-related polypeptide;

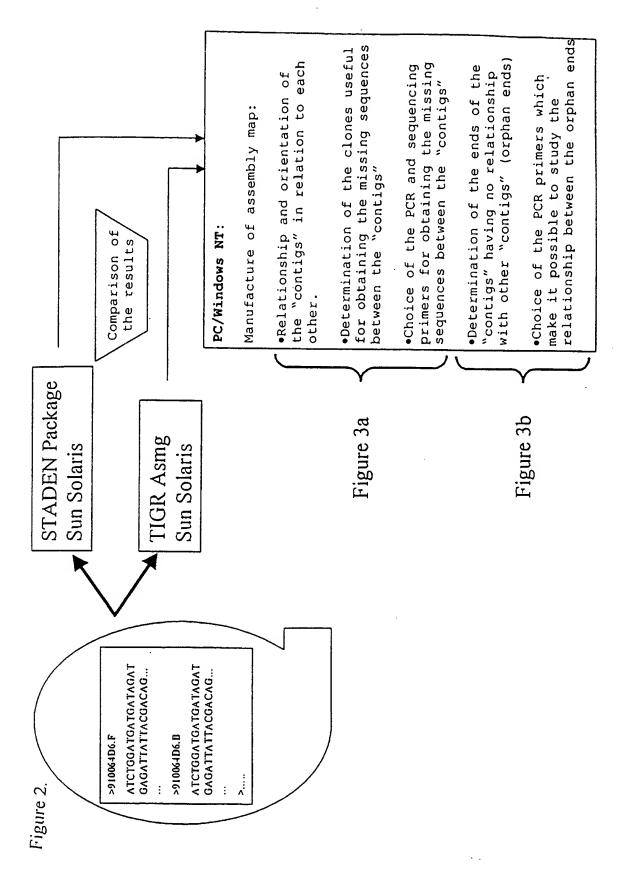
- (u) a Chlamydia trachomatis polypeptide that contains an RGD sequence;
- (v) a Chlamydia trachomatis Type III secreted polypeptide;
- (w) a Chlamydia trachomatis cell wall anchored surface polypeptide; or
- (x) a Chlamydia trachomatis polypeptide that is not found in Chlamydia trachomatis.
- 22. A fusion protein encoded by the polynucleotide of Claim 8.
- 23. The fusion protein of Claim 22 which immunoreacts with seropositive serum of an individual infected with *Chlamydia trachomatis*.
 - 24. An antibody that immunospecifically binds to the polypeptide of Claim 19.
 - 25. An antibody that immunospecifically binds to the fusion protein of Claim 22.
- 26. A method for the detection and/or identification of *Chlamydia trachomatis* in a biological sample, comprising:
 - (a) contacting the sample with a polynucleotide primer of Claim 1, 2, 3, 4, 5, or 6 in the presence of a polymerase enzyme and nucleotides under conditions which permit primer extension; and
 - (b) detecting the presence of primer extension products in the sample in which the detection of primer extension products indicates the presence of *Chlamydia* trachomatis in the sample.
- 27. A method for the detection and/or identification of *Chlamydia trachomatis* in a biological sample, comprising:
 - (a) contacting the sample with a polynucleotide probe of Claim 1, 2, 3, 4, 5, or 6 under conditions which permit hybridization of complementary base pairs; and
 - (b) detecting the presence of hybridization complexes in the sample in which the detection of hybridization complexes indicates the presence of *Chlamydia trachomatis* in the sample.
- 28. A method for the detection and/or identification of *Chlamydia trachomatis* in a biological sample, comprising:
 - (a) contacting the sample with the antibody of Claim 24 under conditions suitable for the formation of immune complexes; and

- (b) detecting the presence of immune complexes in the sample, in which the detection of immune complexes indicates the presence of *Chlamydia trachomatis* in the sample.
- 29. A method for the detection and/or identification of antibodies to *Chlamydia trachomatis* in a biological sample, comprising:
 - (a) contacting the sample with a polypeptide of Claim 19 under conditions suitable for the formation of immune complexes; and
 - (b) detecting the presence of immune complexes in the sample, in which the detection of immune complexes indicates the presence of *Chlamydia trachomatis* in the sample.
- 30. A DNA chip containing an array of polynucleotides comprising at least one of the polynucleotides of Claim 1, 2, 3, 4, 5, or 6.
- 31. A protein chip containing an array of polypeptides comprising at least one of the polypeptides of Claim 19.
- 32. An immunogenic composition comprising the polypeptide of Claim 19 and a pharmaceutically acceptable carrier.
- 33. An immunogeneic composition comprising the polypeptide of Claim 20 and a pharmaceutically acceptable carrier.
- 34. An immunogenic composition comprising the fusion protein of Claim 22 and a pharmaceutically acceptable carrier.
- 35. An immunogenic composition comprising the fusion protein of Claim 23 and a pharmaceutically acceptable carrier.
- 36. A pharmaceutical composition comprising the polypeptide of Claim 19 and a pharmaceutically acceptable carrier.
- 37. A pharmaceutical composition comprising the polypeptide of Claim 20 and a pharmaceutically acceptable carrier.

- 38. A pharmaceutical composition comprising the polypeptide of Claim 22 and a pharmaceutically acceptable carrier.
- 39. A pharmaceutical composition comprising the polypeptide of Claim 23 and a pharmaceutically acceptable carrier.
- 40. A method of immunizing against *Chlamydia trachomatis*, comprising: administering to a host an immunizing amount of the immunogenic composition of Claim 32.
- 41. A method of immunizing against *Chlamydia trachomatis*, comprising: administering to a host an immunizing amount of the immunogenic composition of Claim 33.
- 42. A method of immunizing against *Chlamydia trachomatis*, comprising administering to a host an immunizing amount of the immunogenic composition of Claim 34.
- 43. A method of immunizing against *Chlamydia trachomatis*, comprising: administering to a host an immunizing amount of the immunogenic composition of Claim 35.
- 44. A DNA immunogenic composition comprising the expression vector of Claim 11.
- 45. The DNA composition of Claim 44, wherein the DNA composition directs the expression of a neutralizing epitope of *Chlamydia trachomatis*.
- 46. A DNA immunogenic composition comprising the expression vector of Claim 12.
- 47. The DNA composition of Claim 46, wherein the DNA composition directs the expression of a neutralizing epitope of *Chlamydia trachomatis*.
 - 48. A screening assay, comprising:
 - (a) contacting a test compound with an isolated polynucleotide of Claim 1, 2, 3, 4, 5 or 6; and
 - (b) detecting whether binding occurs.
 - 49. A screening assay, comprising:
 - (a) contacting a test compound with the polypeptide of Claim 19; and

- (b) detecting whether binding occurs.
- 50. A screening assay, comprising:
- (a) contacting a test compound with the polypeptide of Claim 22; and
- (b) detecting whether binding occurs.
- 51. A kit comprising a container containing an isolated polynucleotide of Claim 1, 2, 3, 4, 5 or 6.
 - 52. The kit of Claim 51 wherein the polynucleotide is a primer or a probe.
- 53. The kit of Claim 51 wherein the polynucleotide is a primer and the kit further comprises a container containing a polymerase.
- 54. The kit of Claim 51 which further comprises a container containing deoxynucleotide triphosphates.
- 55. A kit comprising a container containing an antibody that immunospecifically binds to the polypeptide of Claim 19.
- 56. A kit comprising a container containing an antibody that immunospecifically binds to the fusion protein of Claim 22.





2- Define the PCR primers which make it possible to fill

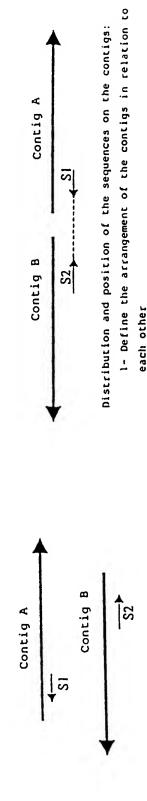
the sequence

Statistical determination of the sequences:

1- Belonging to the same clone

2- Situated on two different contigs

FIGURE 3A



Contig A S Contig B 22 Ct18 CtI Contig D \$5 2- Determination of outer and inner PCR Contig ends without connecting clone: S4 Contig C 1- Identification of the ends

FIGURE 3B

E: outer primers

between the contigs

primers for studying the relationships

1: inner primers

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

□ BLACK BORDERS
□ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
□ FADED TEXT OR DRAWING
□ BLURRED OR ILLEGIBLE TEXT OR DRAWING
□ SKEWED/SLANTED IMAGES
□ COLOR OR BLACK AND WHITE PHOTOGRAPHS
□ GRAY SCALE DOCUMENTS
□ LINES OR MARKS ON ORIGINAL DOCUMENT
□ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

IMAGES ARE BEST AVAILABLE COPY.

☐ OTHER: _____

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.

THIS PAGE BLANK (USPTO)